

## AMENDMENTS TO THE CLAIMS

Please add claims 161-270 as indicated below.  
This listing of claims will replace all prior versions,  
and listings, of claims in the application:

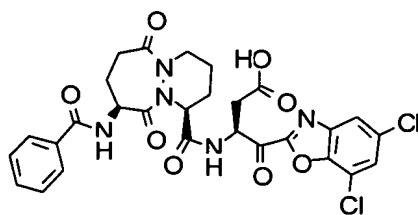
5 Listing of Claims:

1-37. (canceled)

38. (previously presented) The compound according to claims 62 or 68, selected from the group consisting of:

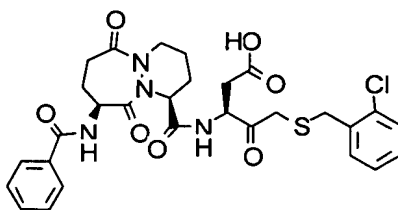


223e



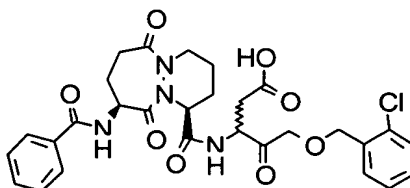
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226e



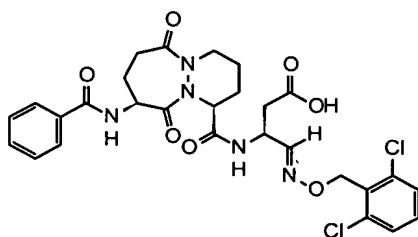
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227e



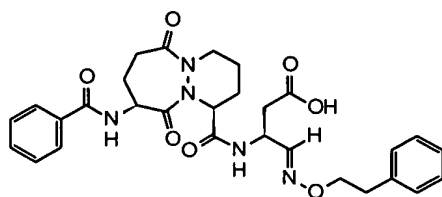
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307a



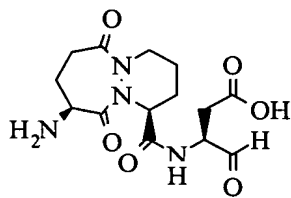
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307b



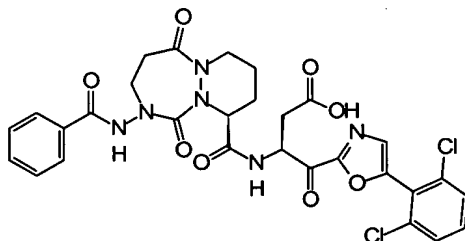
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429



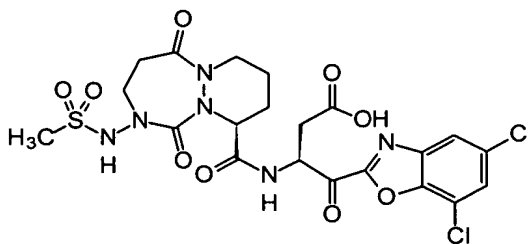
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820b



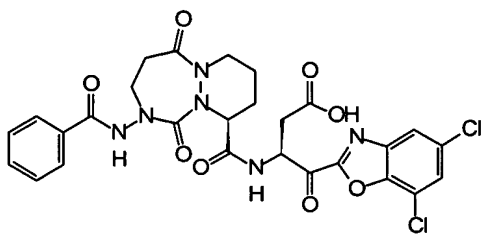
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823b



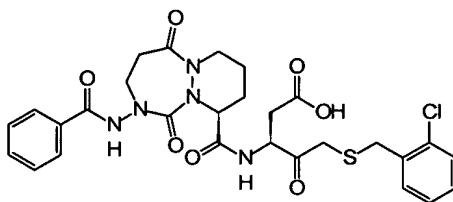
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823e



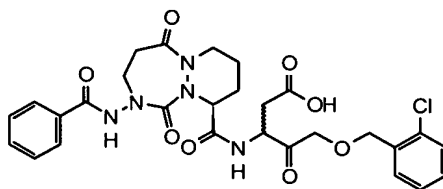
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826e



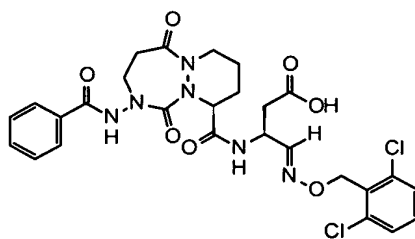
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827e



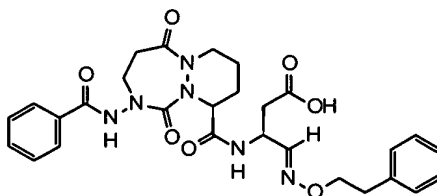
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907a



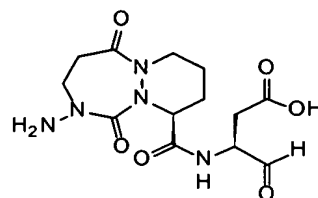
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907b



; and

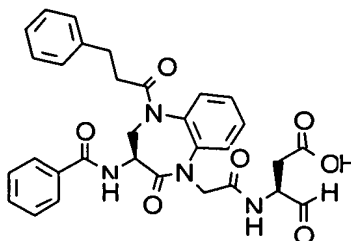
1029



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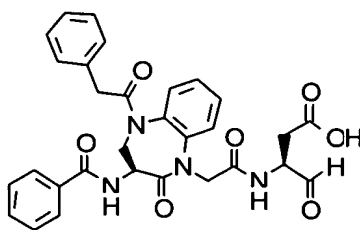
39. (previously presented) The compound  
according to claim 62, selected from the group  
5 consisting of:

605a



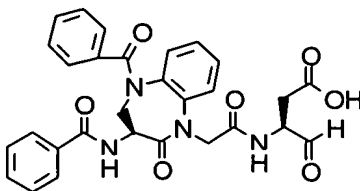
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605b



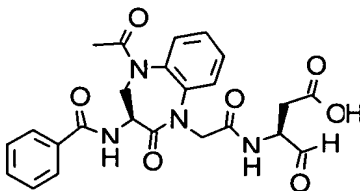
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605c



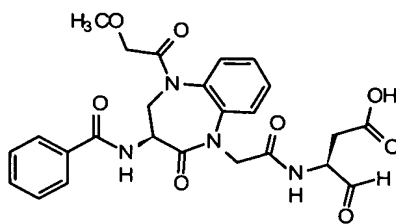
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605d



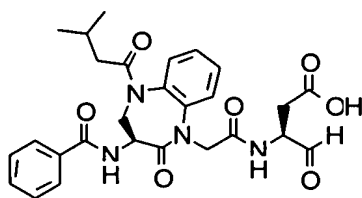
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605e



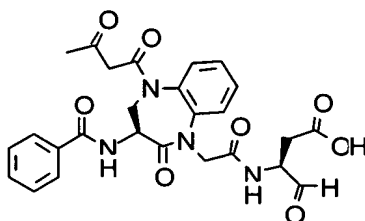
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605f



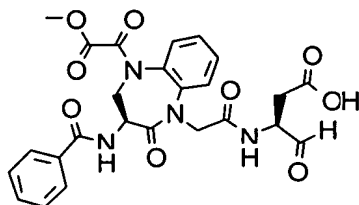
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605g



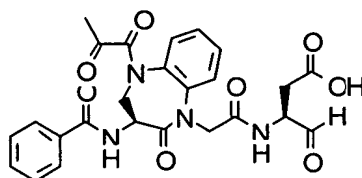
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605h



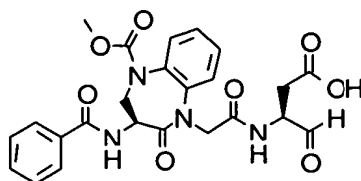
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605i



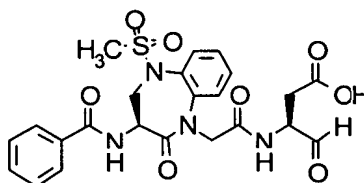
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605j



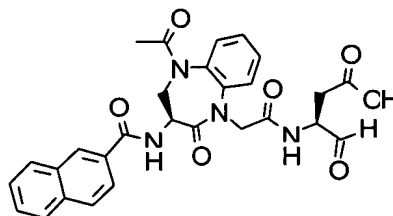
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605m



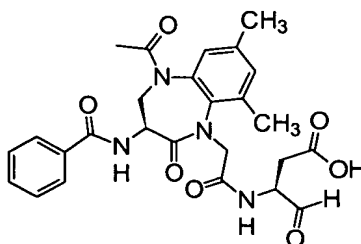
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605n



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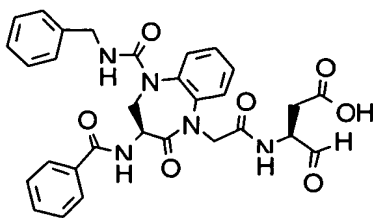
605o



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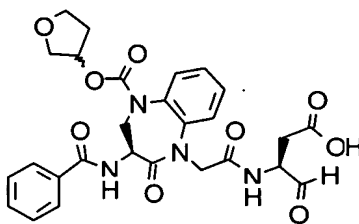


605p



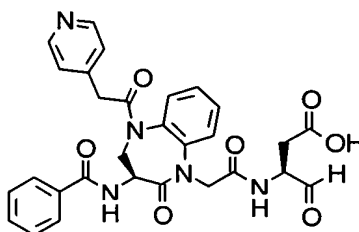
2

605q



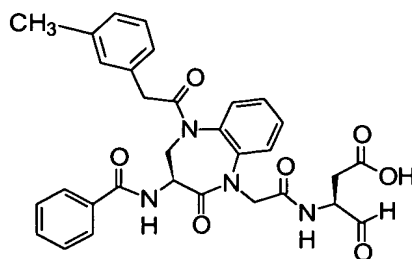
**i**

605s



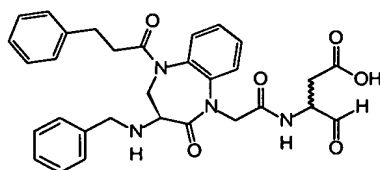
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605t



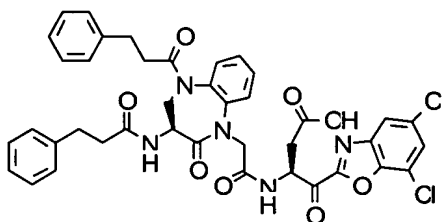
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605v



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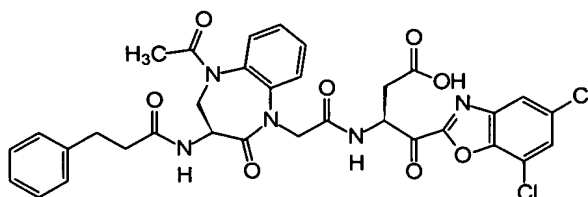
609a



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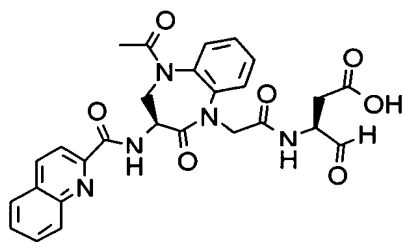
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609b



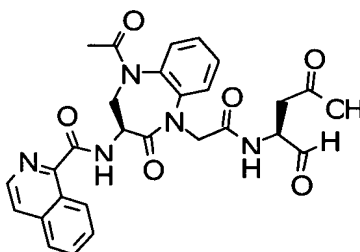
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619



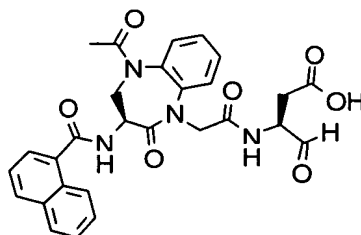
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620



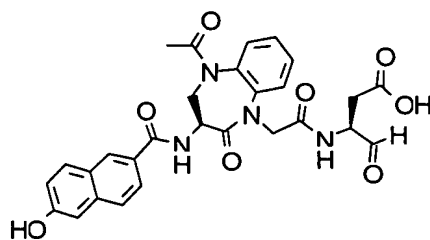
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621



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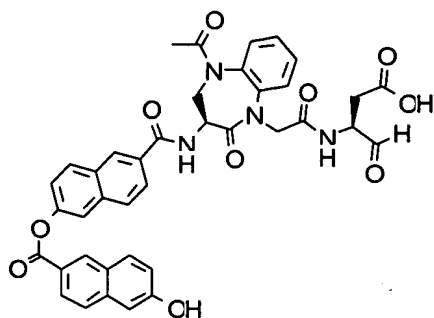
622



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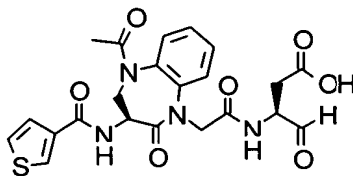
Application No. 10/058,522  
Supp. Amdt. dated March 11, 2004

623



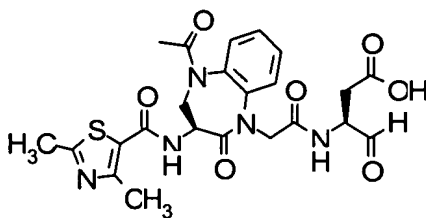
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624



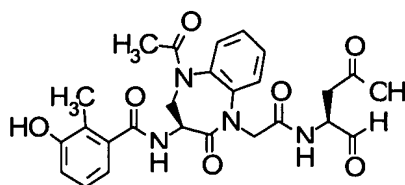
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625

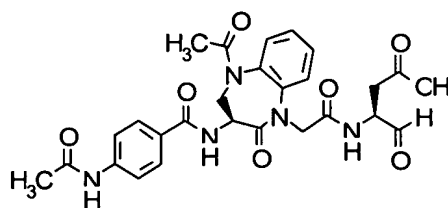


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626

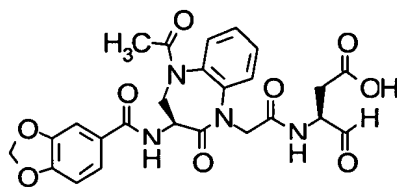
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627

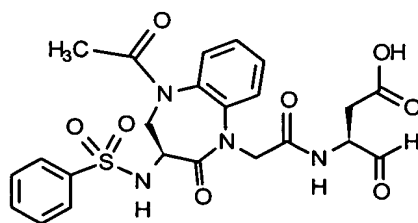


7

628

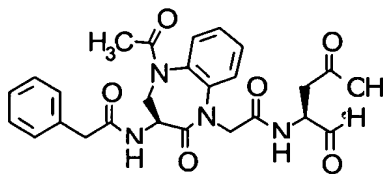
*i*

629

*i*

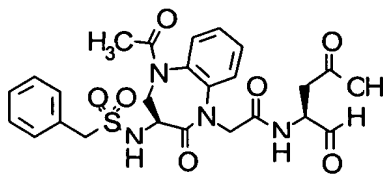
Application No. 10/058,522  
Supp. Amdt. dated March 11, 2004

630



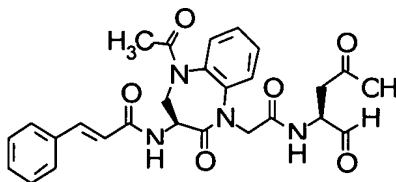
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631



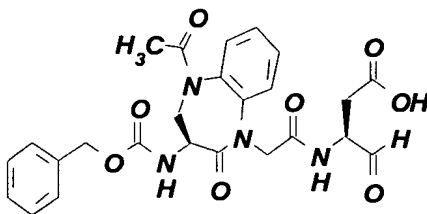
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632



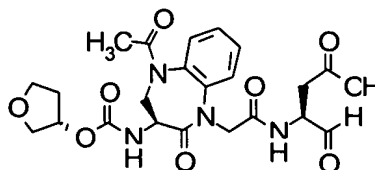
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633



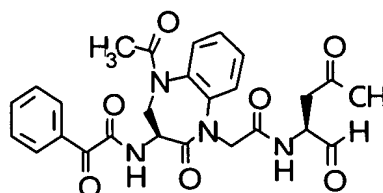
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634



; and

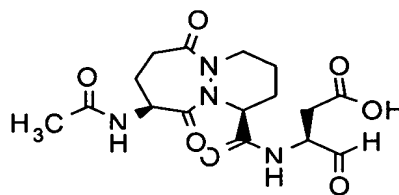
635



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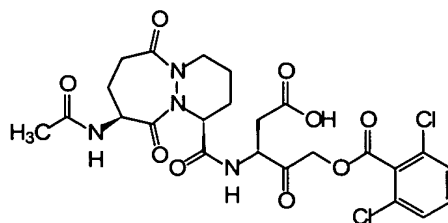
40. (previously presented) The compound  
according to claims 62 or 68, selected from the group  
5 consisting of:

214c



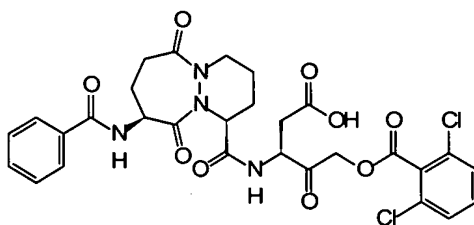
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217c



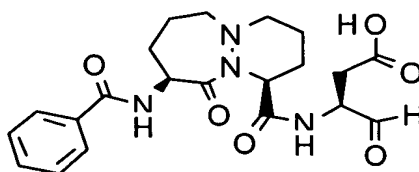
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217e



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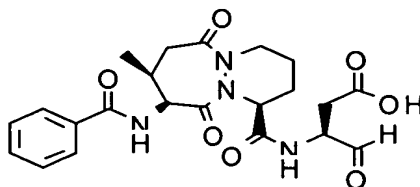
246



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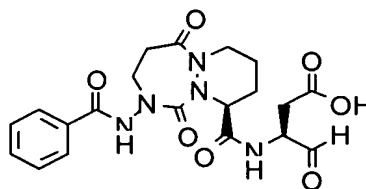


257



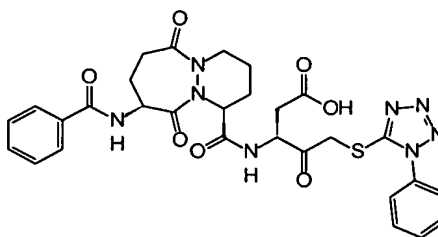
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265



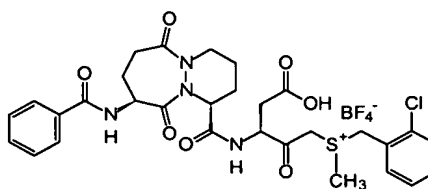
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280

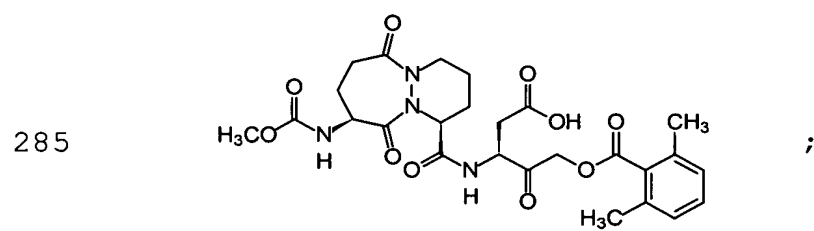
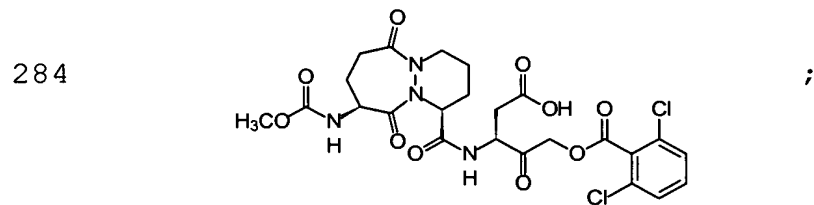
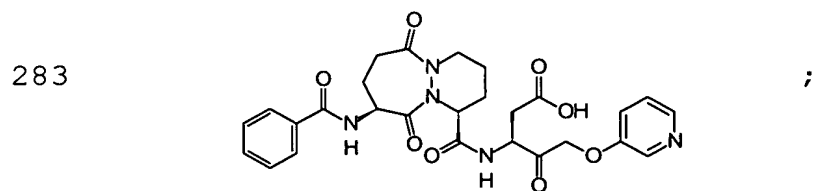
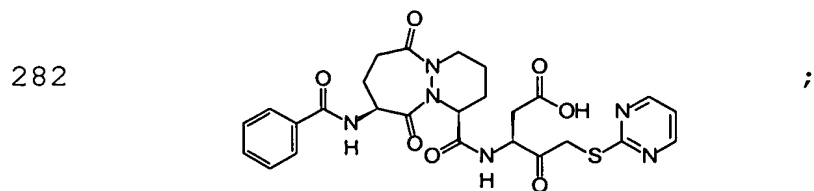


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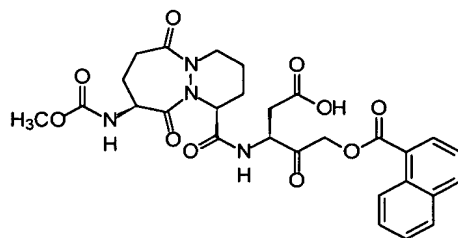
281



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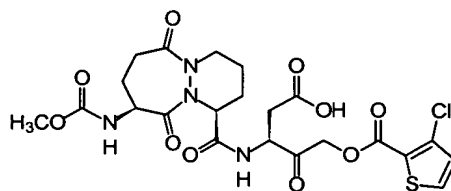


286



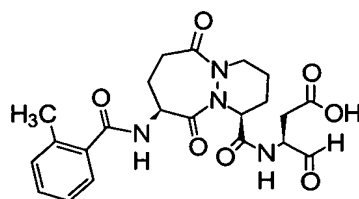
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287



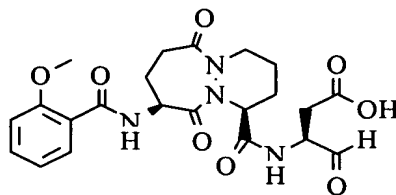
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404



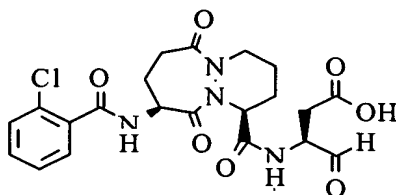
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405



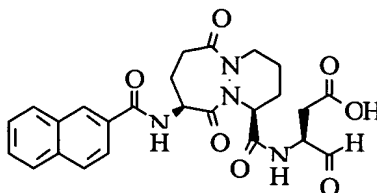
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406



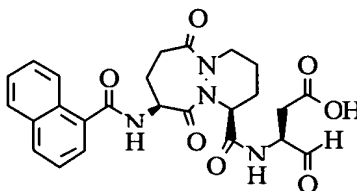
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407



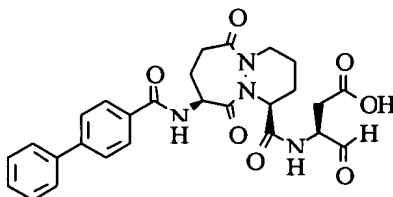
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408



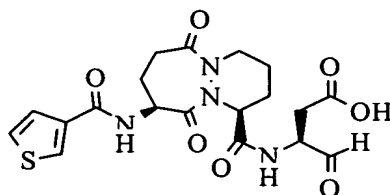
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409



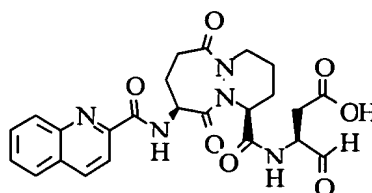
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410



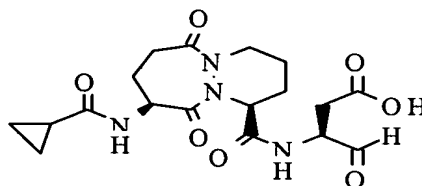
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411



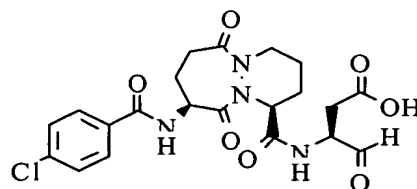
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413



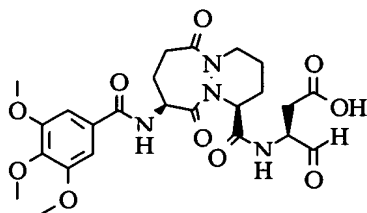
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416



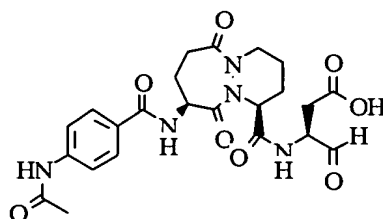
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417



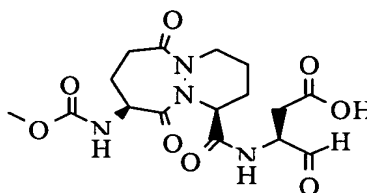
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418



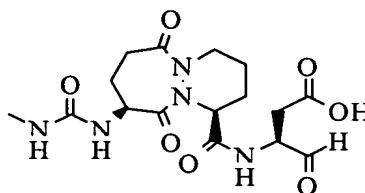
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419



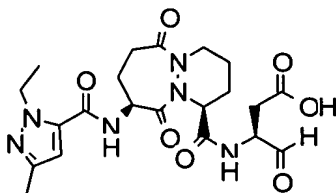
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420



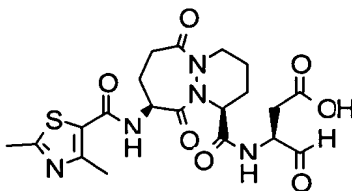
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422



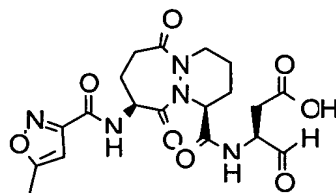
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423



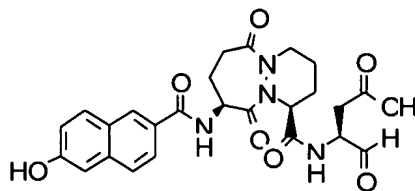
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424



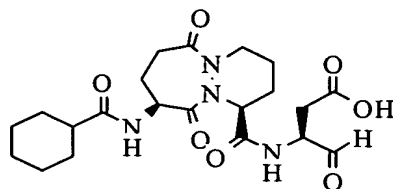
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425



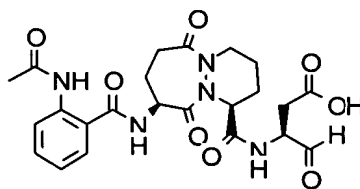
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426



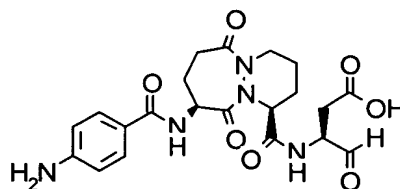
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430



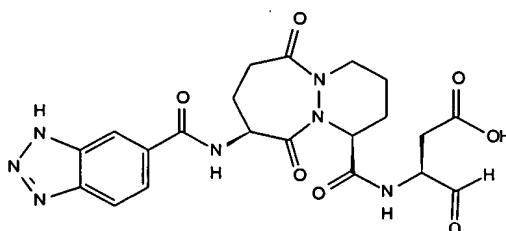
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431



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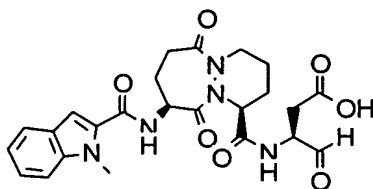
432



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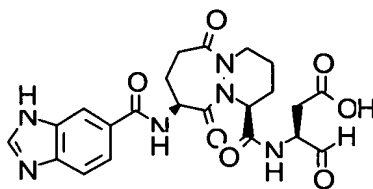


433



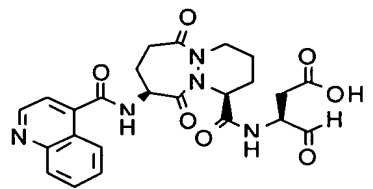
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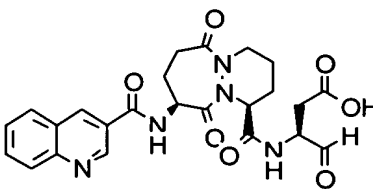
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435



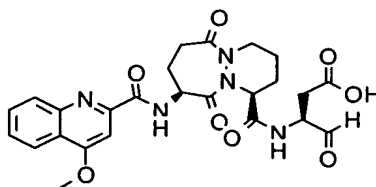
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436



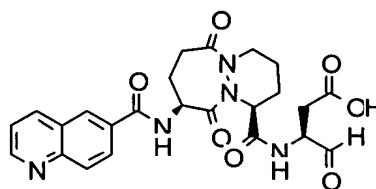
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437



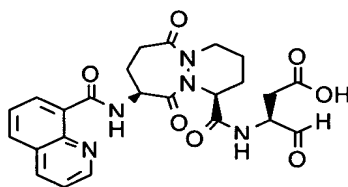
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438



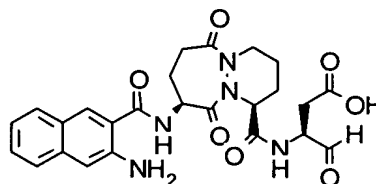
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439



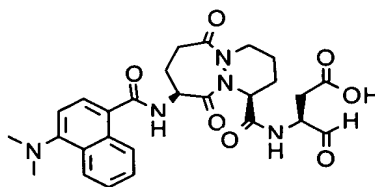
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440



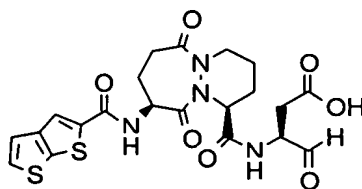
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441



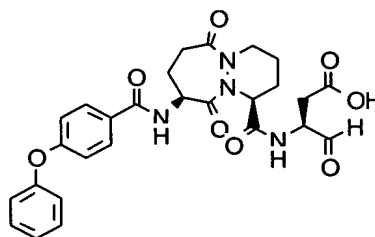
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442



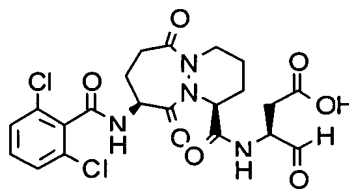
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443



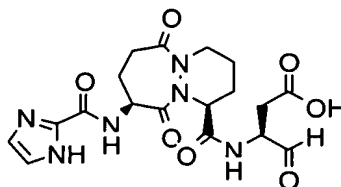
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444



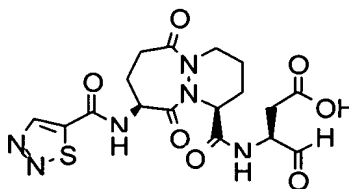
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445



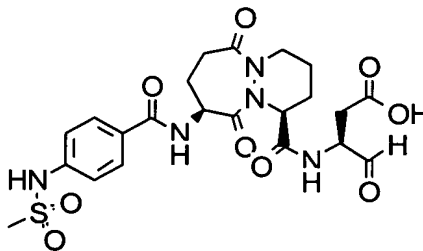
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446



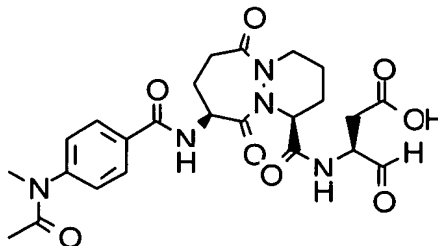
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447



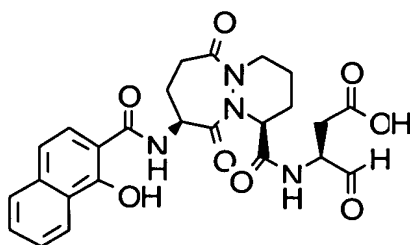
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448



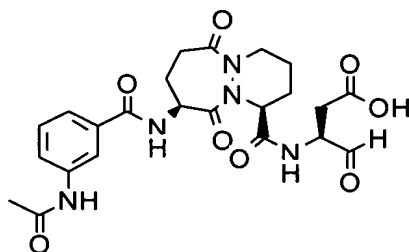
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449



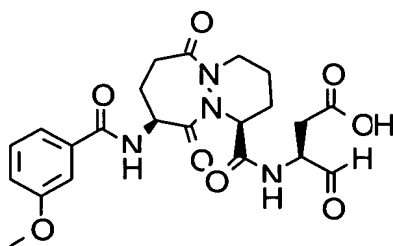
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450



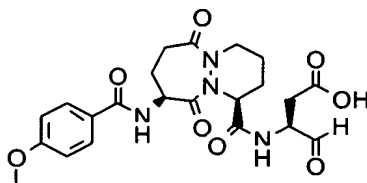
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451



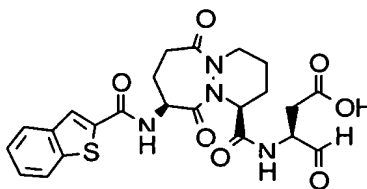
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452



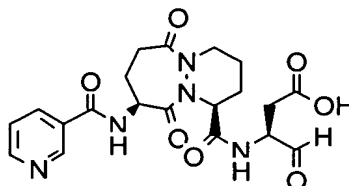
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453



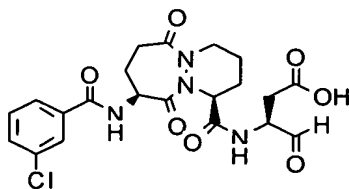
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454



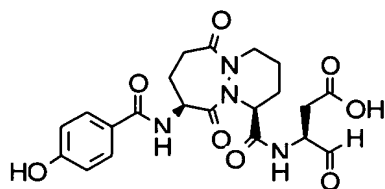
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455



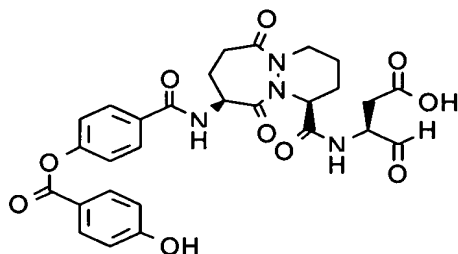
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456



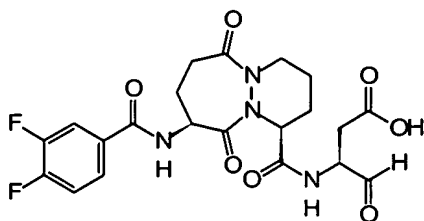
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457



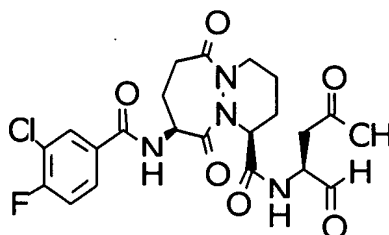
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458



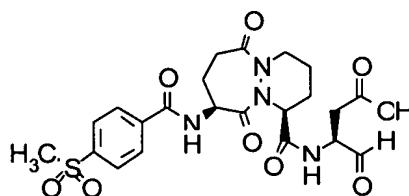
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459



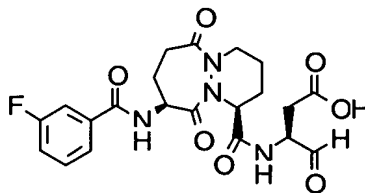
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460



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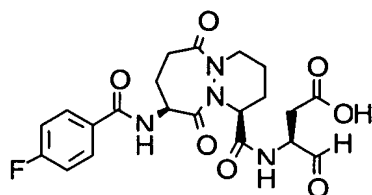
462



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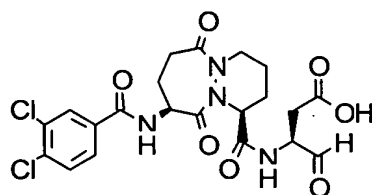


463



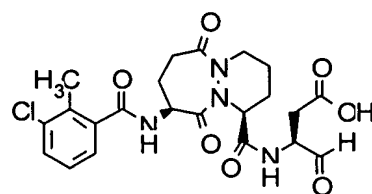
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464



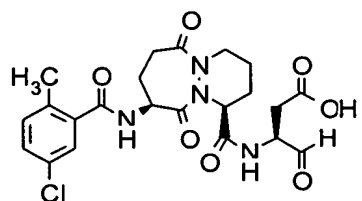
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465



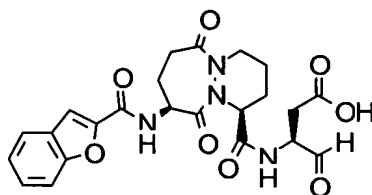
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466



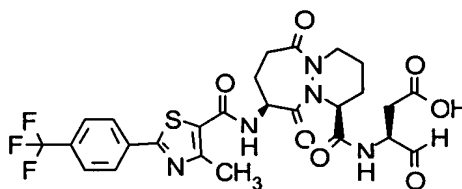
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467



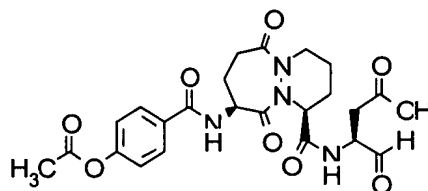
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468



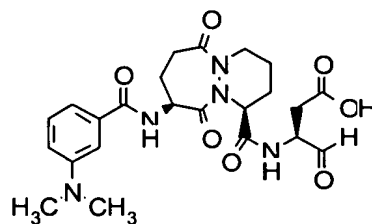
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469



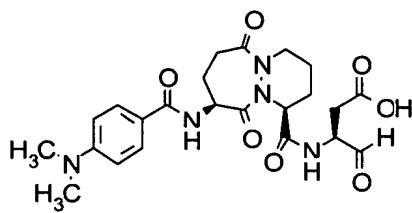
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470



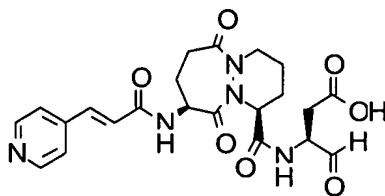
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471



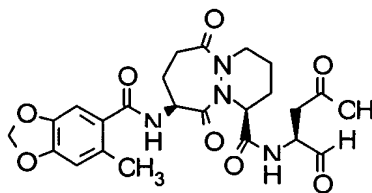
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472



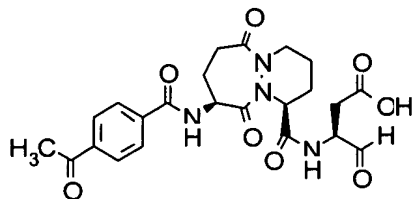
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473



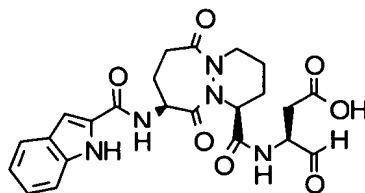
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474



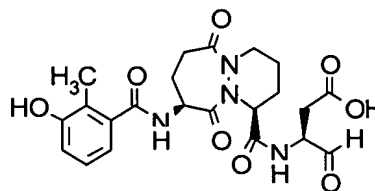
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475



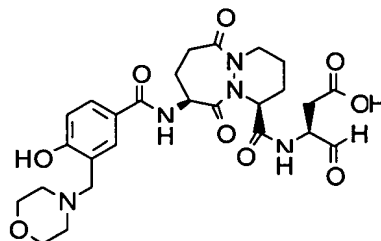
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476



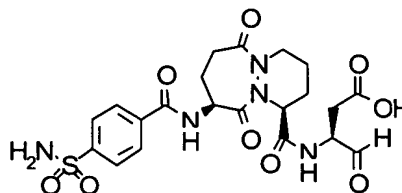
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477



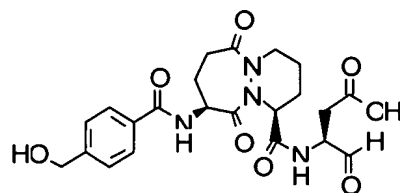
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478



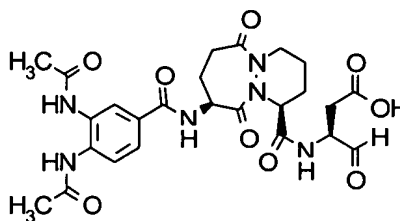
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479



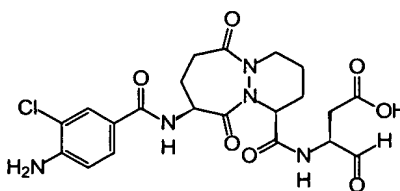
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480



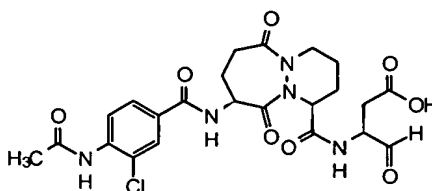
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481



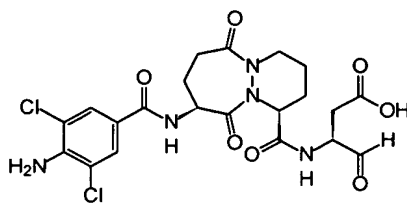
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481s



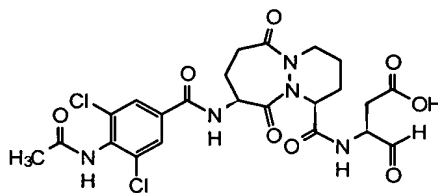
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482



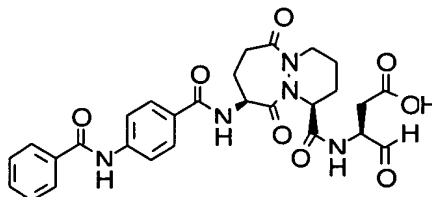
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482s



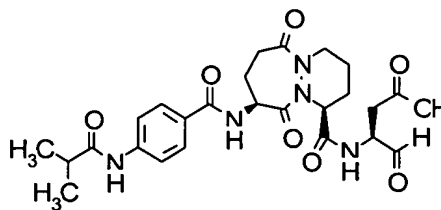
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483



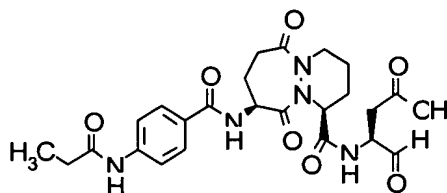
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484



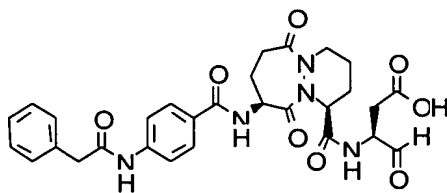
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485



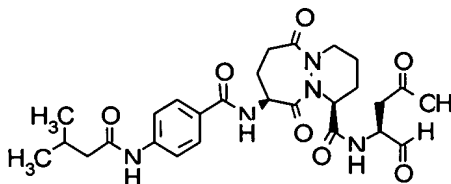
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486



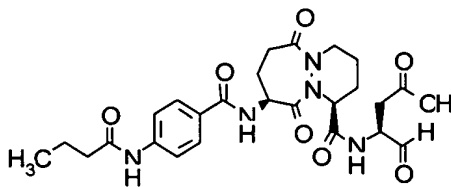
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487



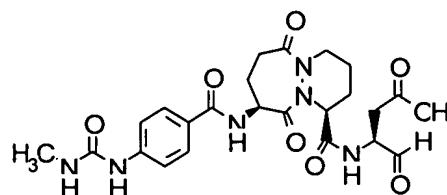
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488



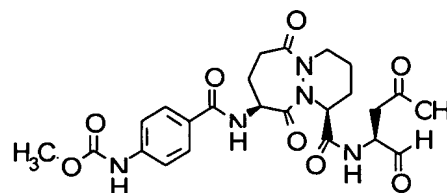
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489



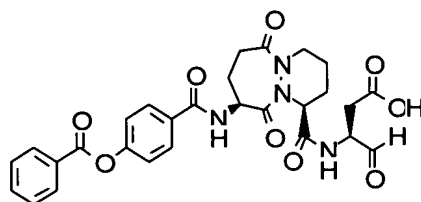
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490



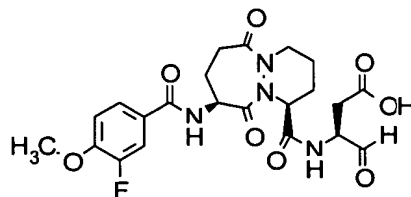
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491



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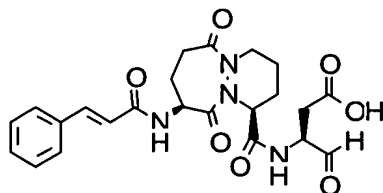
493



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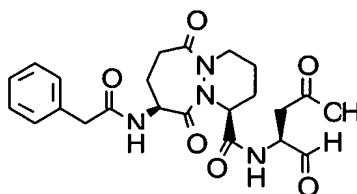


494



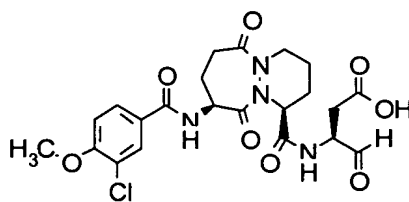
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495



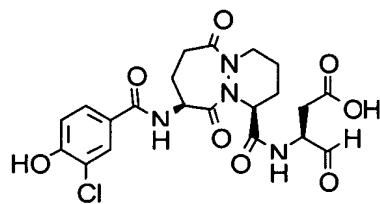
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497



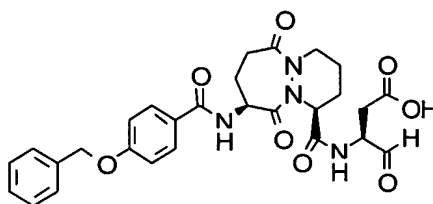
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498



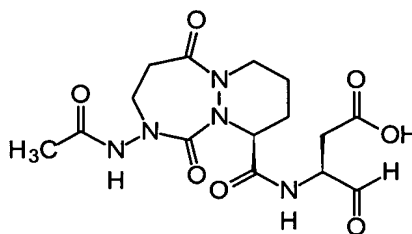
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499



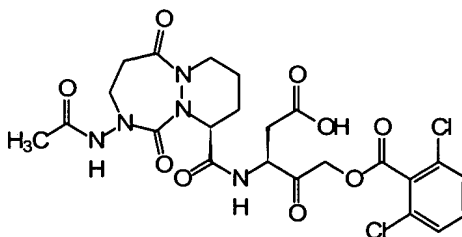
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814c



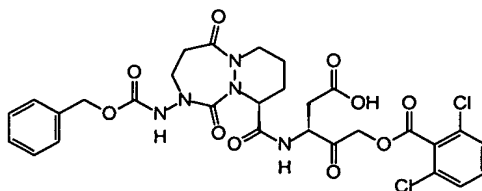
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817c



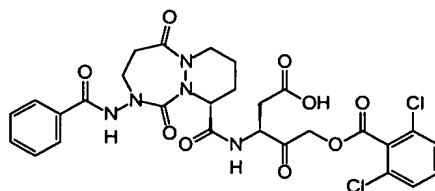
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817d



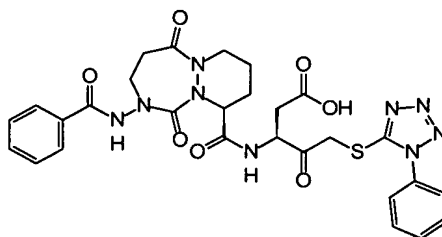
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817e



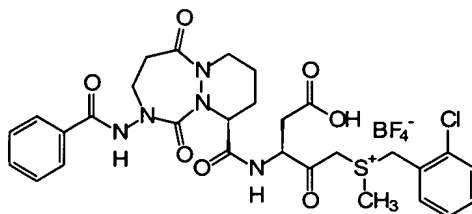
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880



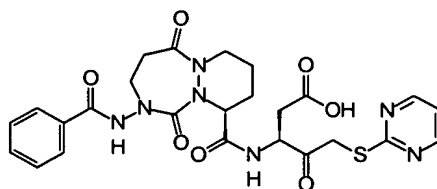
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881



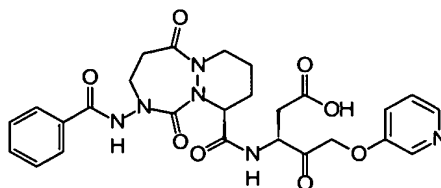
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882



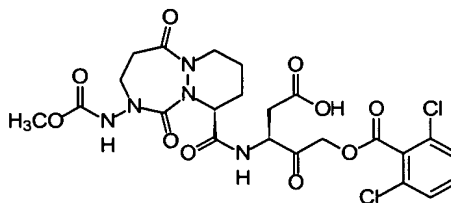
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883



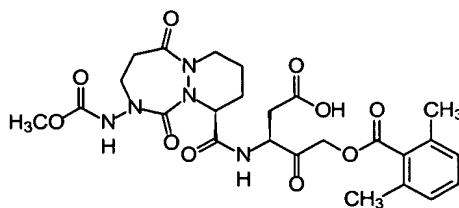
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884



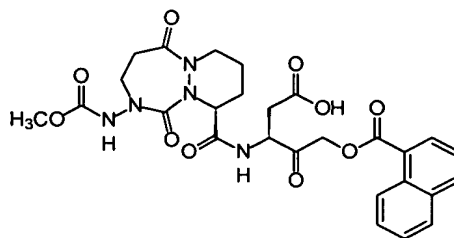
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885



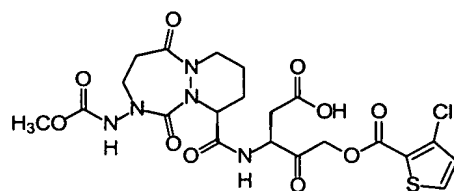
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886



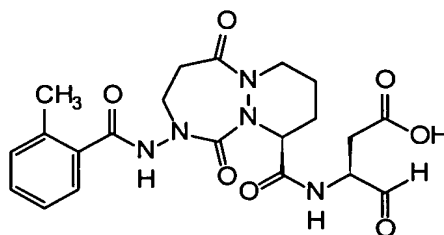
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887



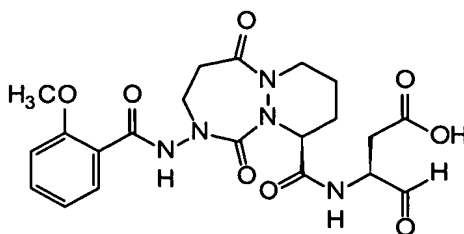
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1004

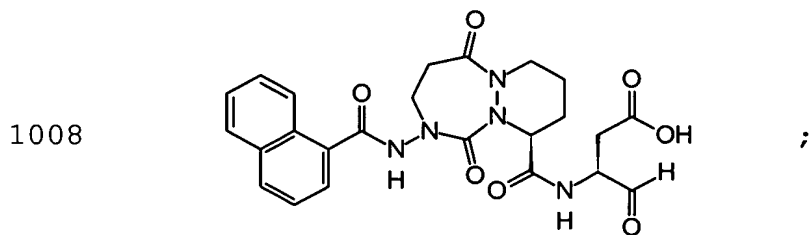
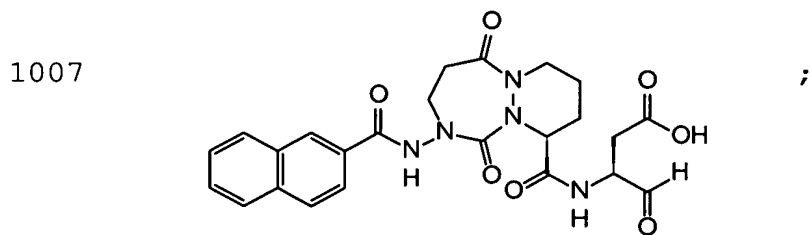
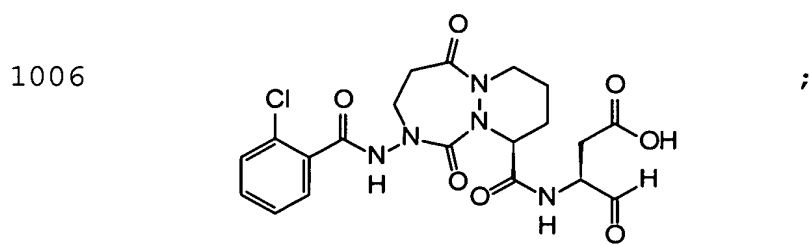


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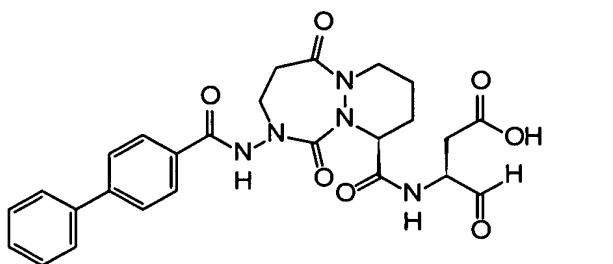
1005



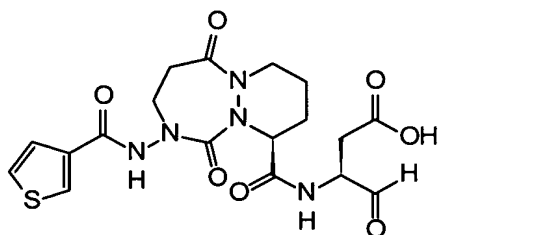
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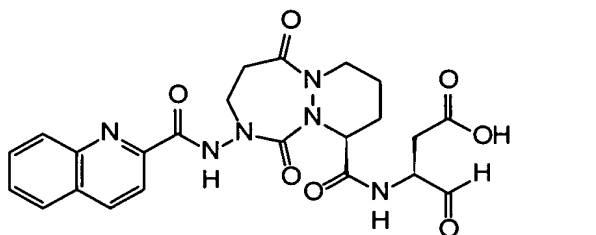
1009



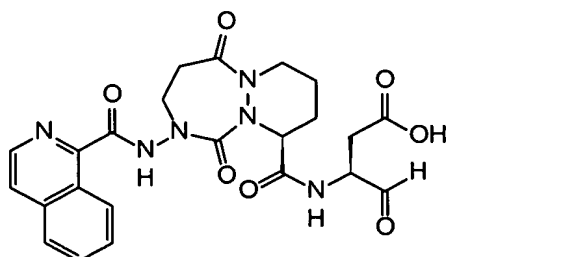
1010



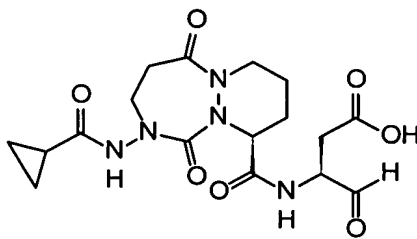
1011



1012

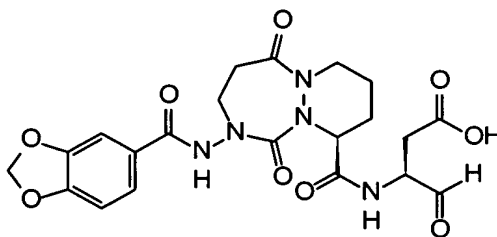


1013



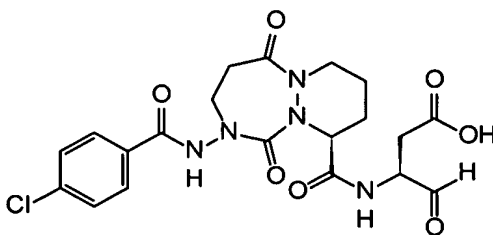
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1015



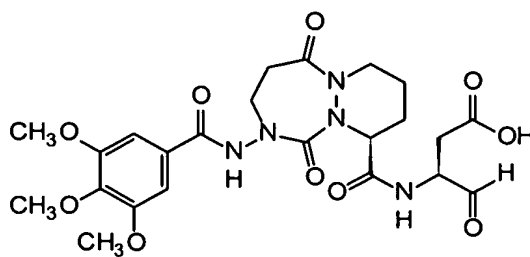
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1016



;

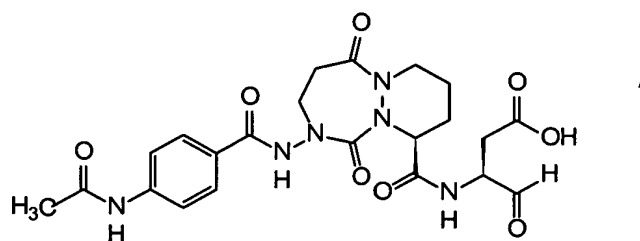
1017



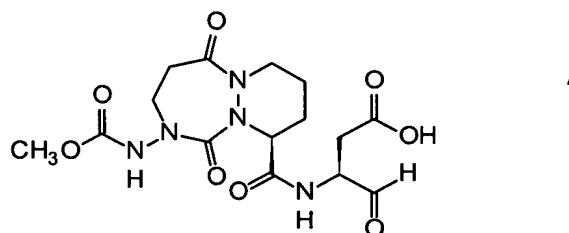
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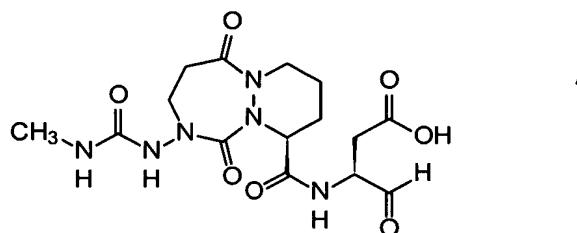
1018



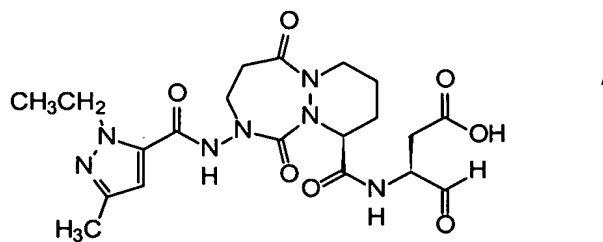
1019



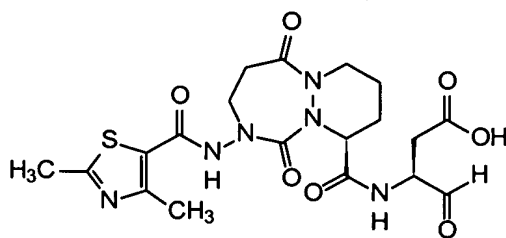
1020



1022

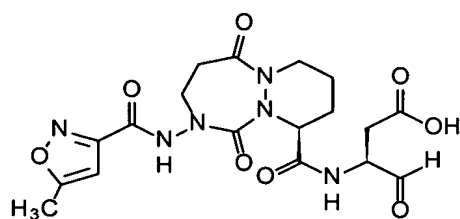


1023



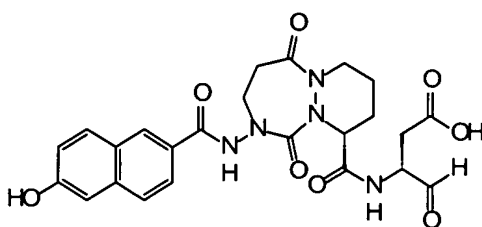
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1024



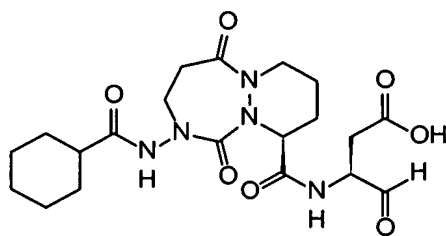
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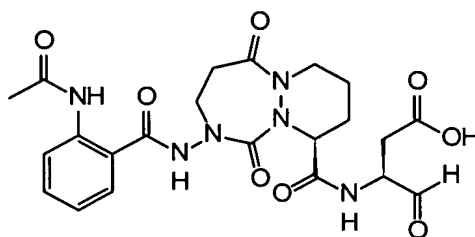
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1026



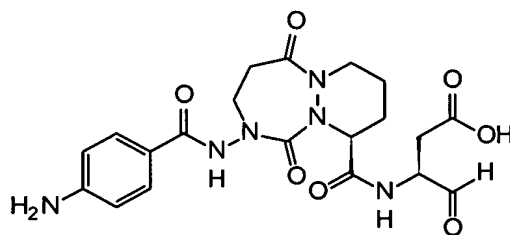
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1030



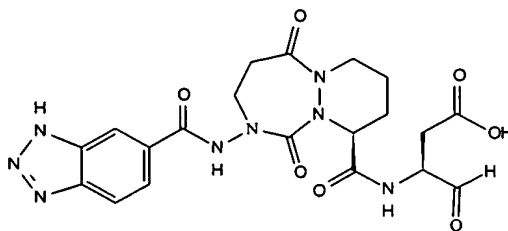
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1031



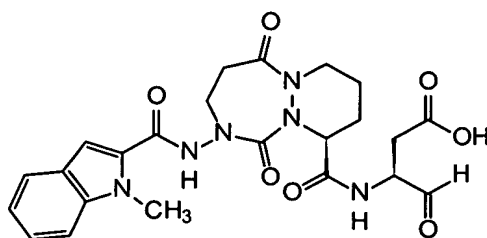
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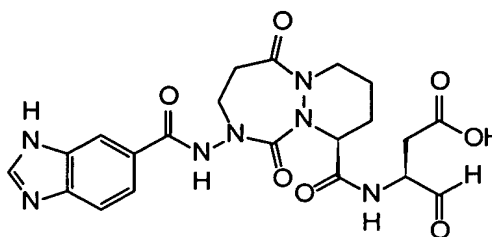
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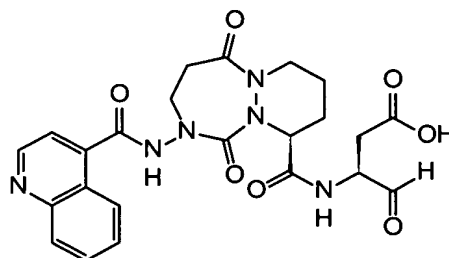
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1034



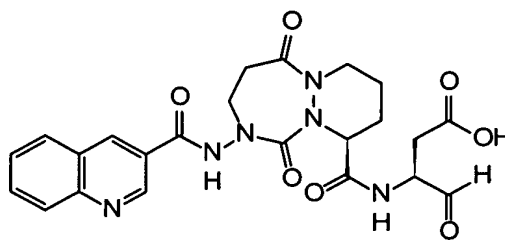
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1035



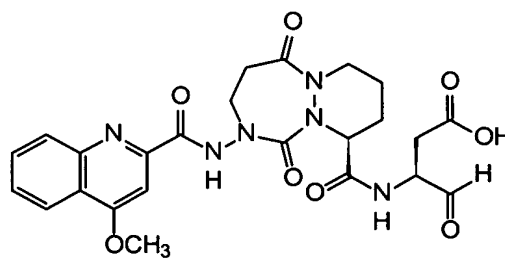
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1036



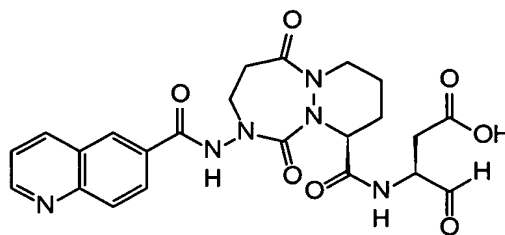
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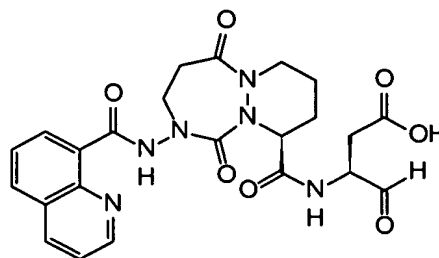
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1038



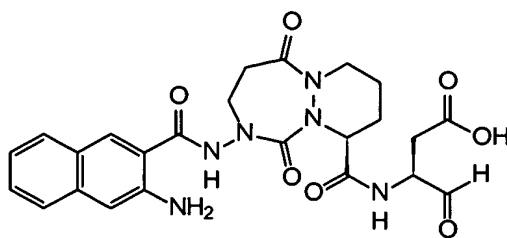
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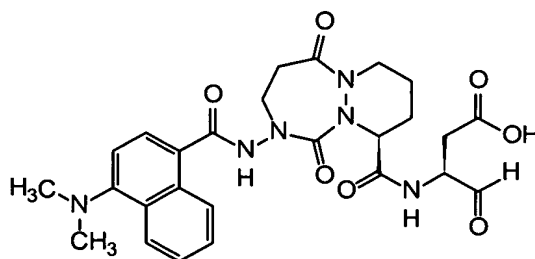


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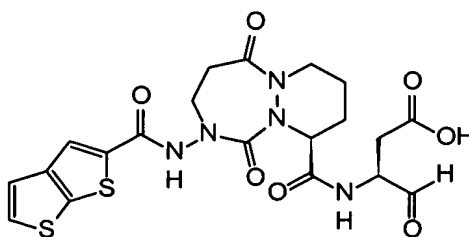
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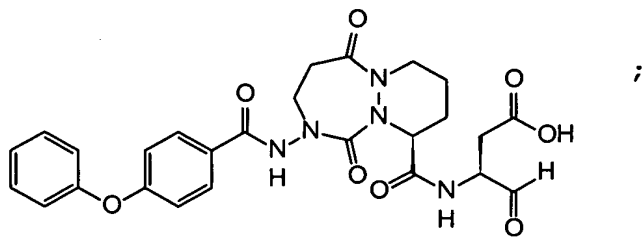


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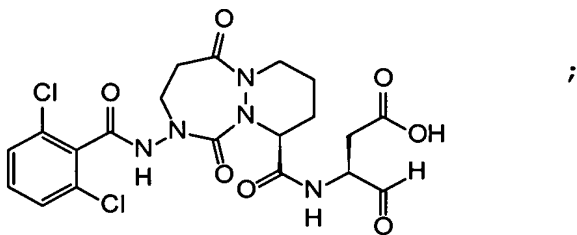


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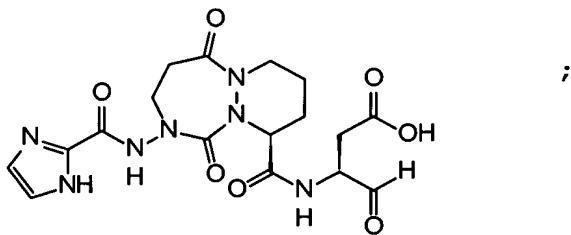
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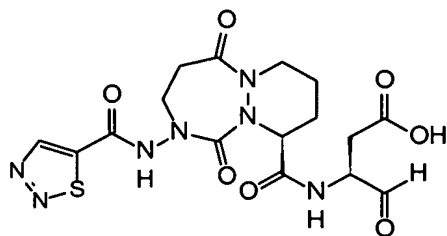
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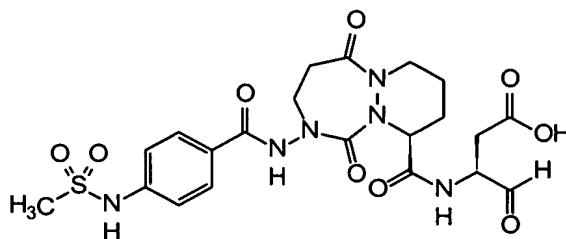


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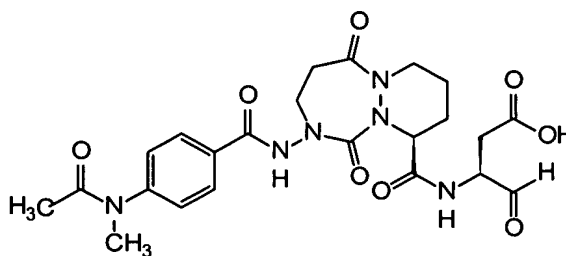
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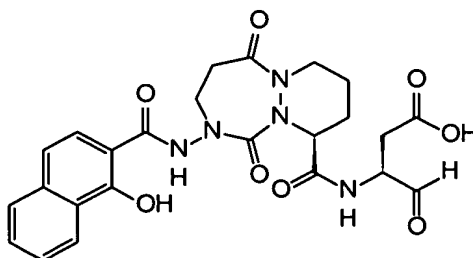
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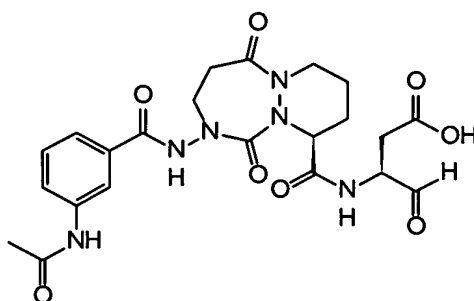
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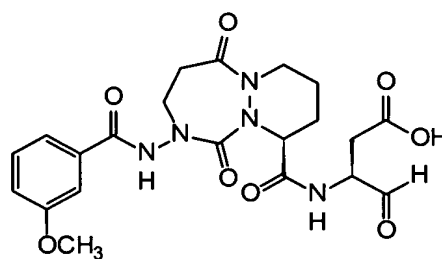


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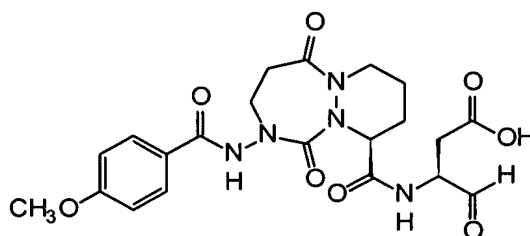
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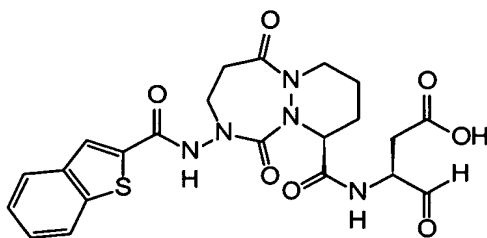
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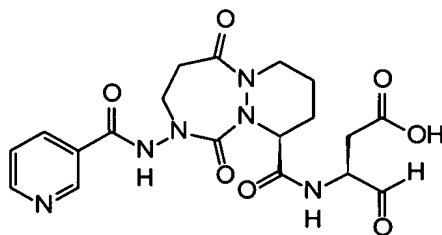
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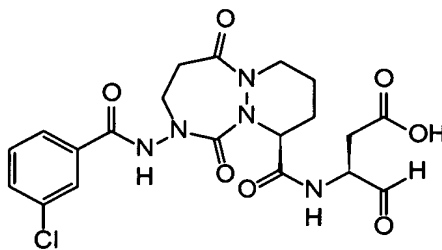
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1054



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1055



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1056

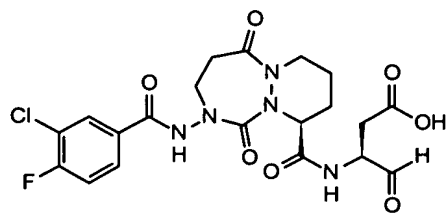


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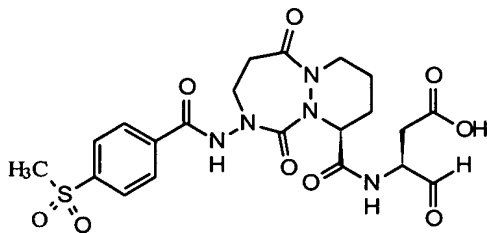
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1059



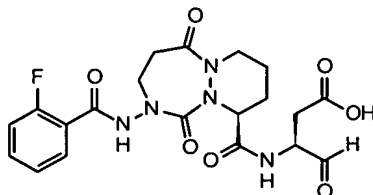
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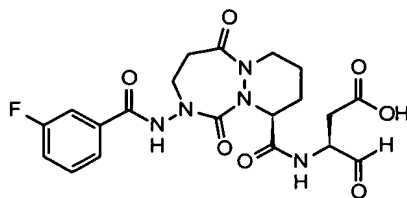
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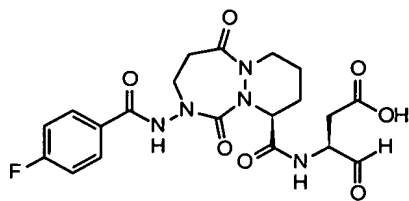
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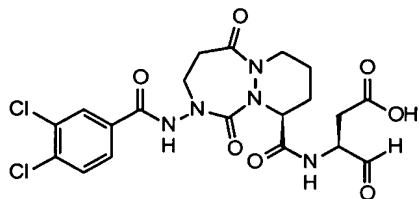
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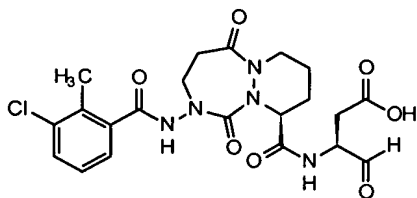
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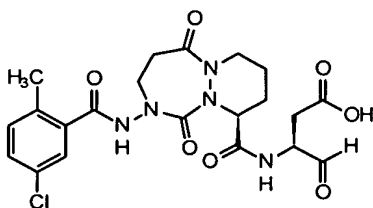
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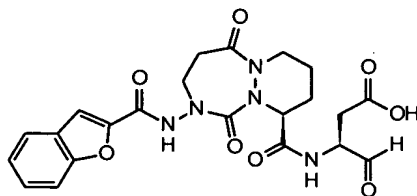
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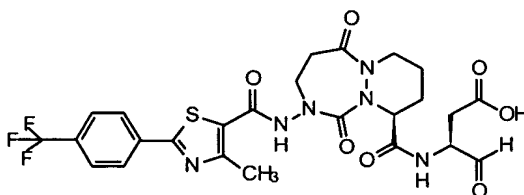
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1067



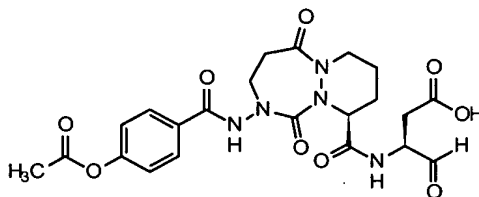
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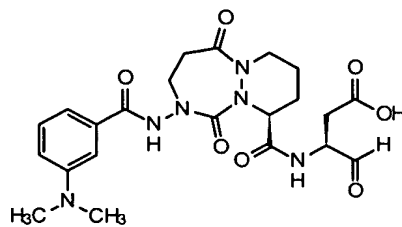
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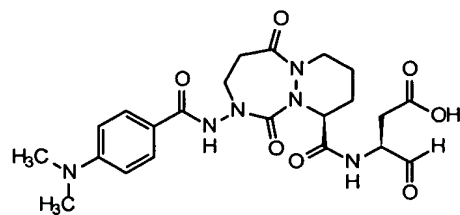
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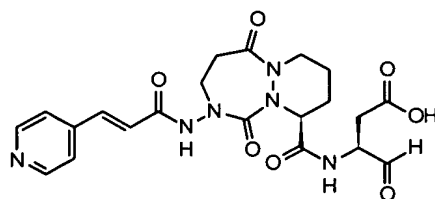
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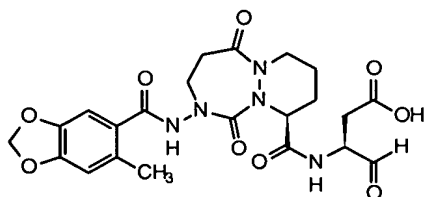
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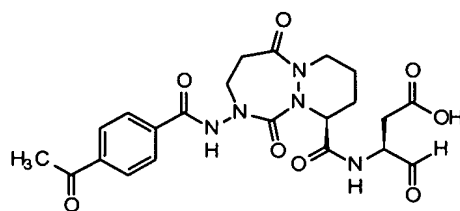
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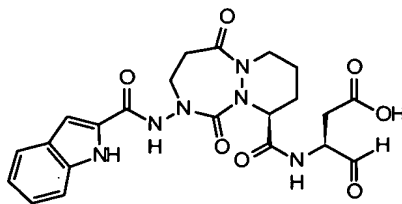
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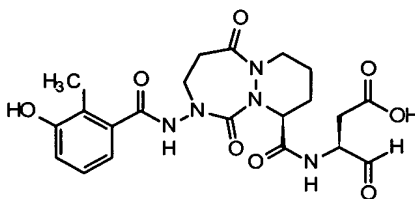
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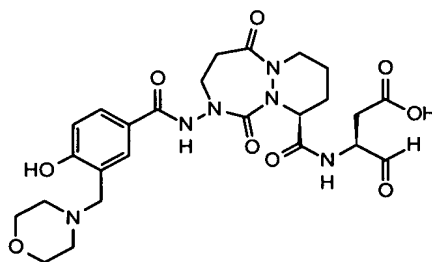
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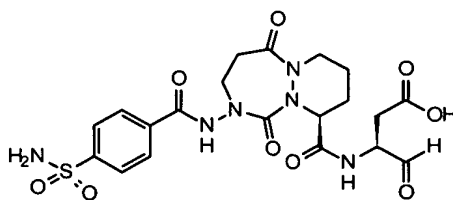
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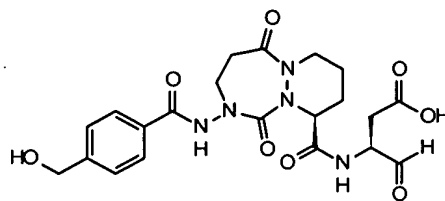
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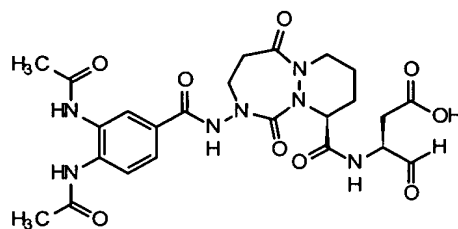


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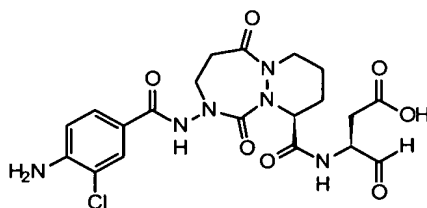
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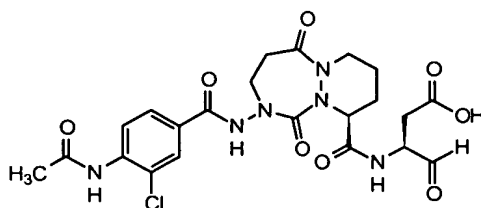
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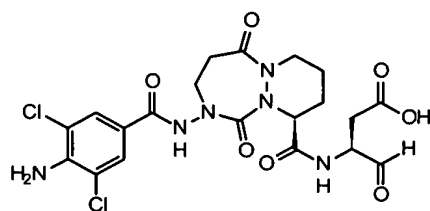
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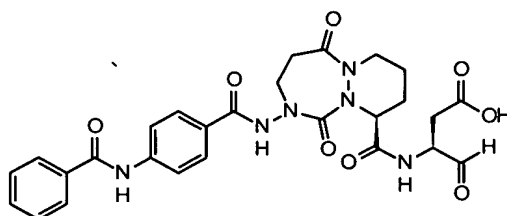
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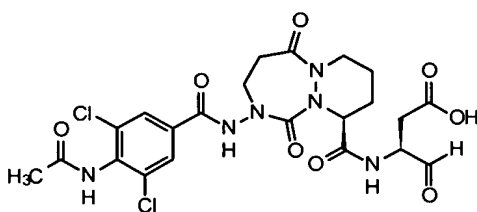
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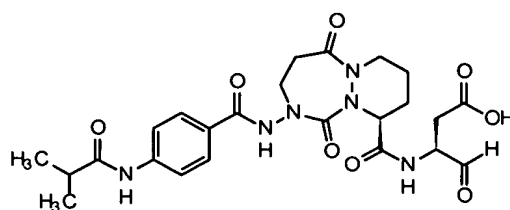
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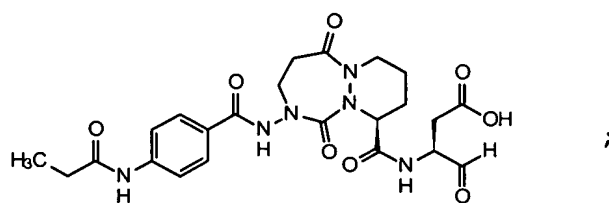
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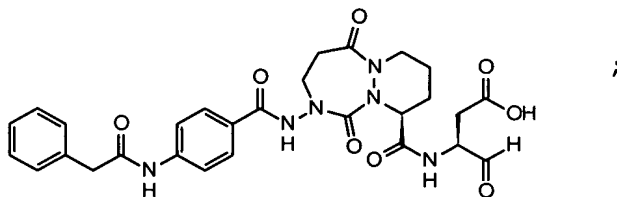


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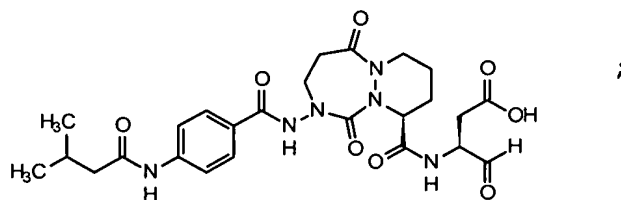
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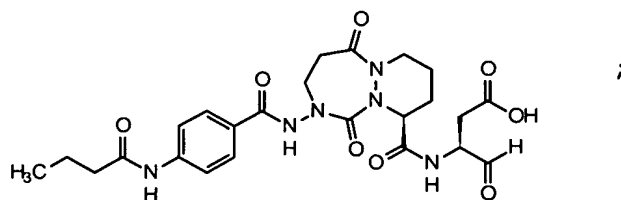
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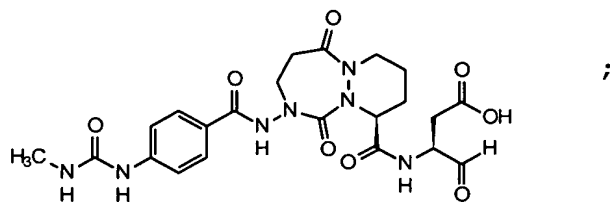
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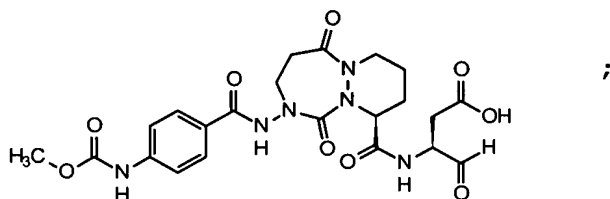
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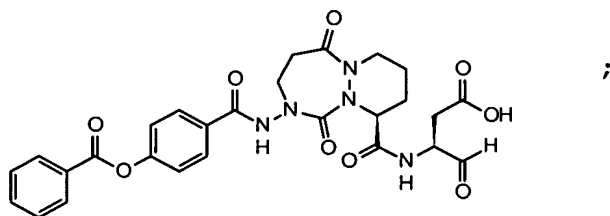
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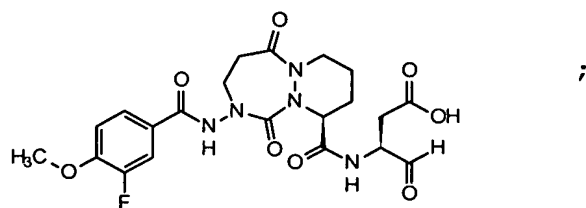
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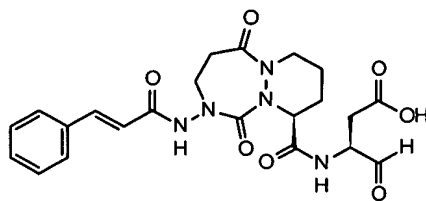
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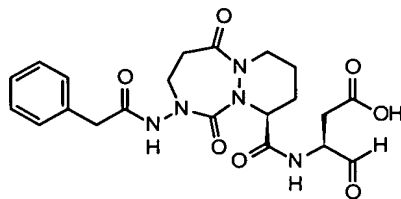
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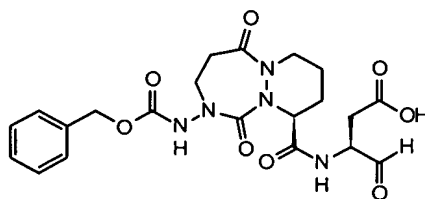
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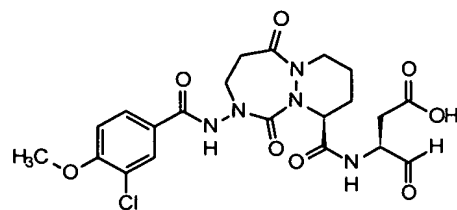
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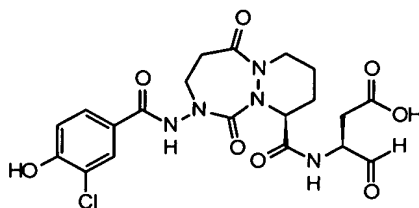
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1097

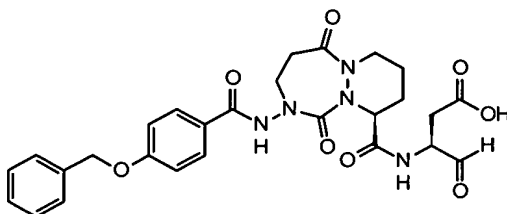


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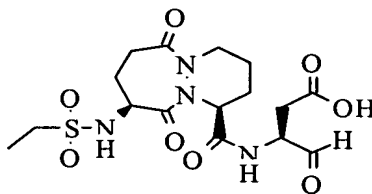
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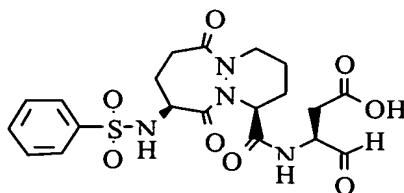
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421



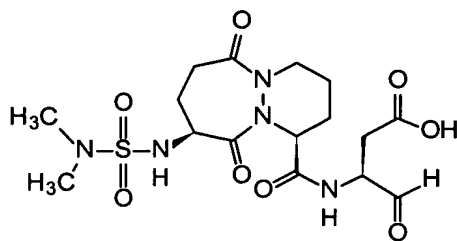
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427



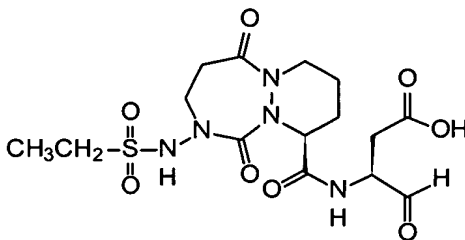
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428



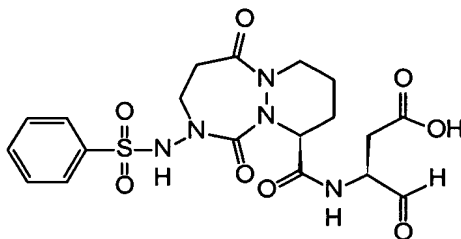
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1021



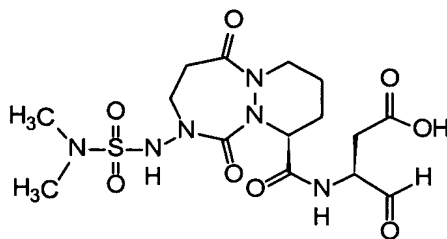
;

1027



; and

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.

41. (canceled)

42. (previously presented) A pharmaceutical composition comprising a compound according to any one

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of claims 38-40, 57, 62, 66, 68, 79-83, 88-93, 95, 96,  
98, 99, 100, 102, 104, 112, 114, 118-131, 133-135 and a  
pharmaceutically acceptable carrier.

43-54. (canceled)

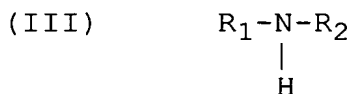
5                   55. (previously presented) A method for  
treating or preventing a disease selected from the  
group consisting of an IL-1 mediated disease, an  
apoptosis mediated disease, an inflammatory disease, an  
autoimmune disease, a destructive bone disorder, a  
10   proliferative disorder, an infectious disease, a  
degenerative disease, a necrotic disease,  
osteoarthritis, pancreatitis, asthma, adult respiratory  
distress syndrome, glomerulonephritis, rheumatoid  
arthritis, systemic lupus erythematosus, scleroderma,  
15   chronic thyroiditis, Grave's disease, autoimmune  
gastritis, insulin-dependent diabetes mellitus (Type  
I), autoimmune hemolytic anemia, autoimmune  
neutropenia, thrombocytopenia, chronic active  
hepatitis, myasthenia gravis, inflammatory bowel  
20   disease, Crohn's disease, psoriasis, graft vs host  
disease, osteoporosis, multiple myeloma-related bone  
disorder, acute myelogenous leukemia, chronic  
myelogenous leukemia, metastatic melanoma, Kaposi's



sarcoma, multiple myeloma, sepsis, septic shock,  
Shigellosis, Alzheimer's disease, Parkinson's disease,  
cerebral ischemia, myocardial ischemia, spinal muscular  
atrophy, multiple sclerosis, AIDS-related encephalitis,  
5 HIV-related encephalitis, aging, alopecia, and  
neurological damage due to stroke in a patient  
comprising the step of administering to said patient a  
pharmaceutical composition according to claim 42.

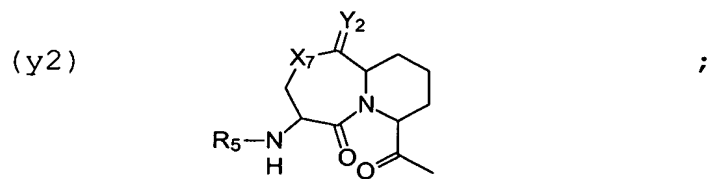
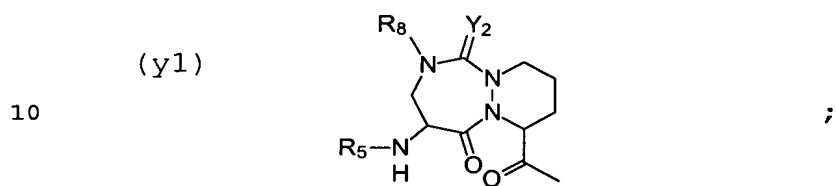
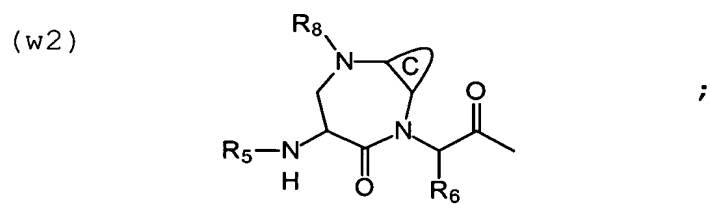
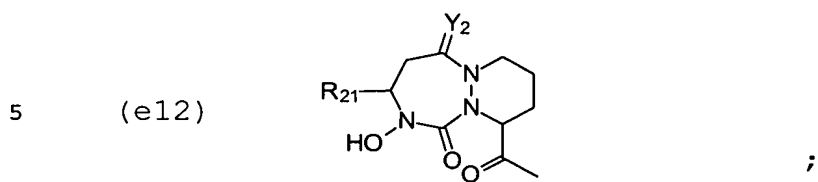
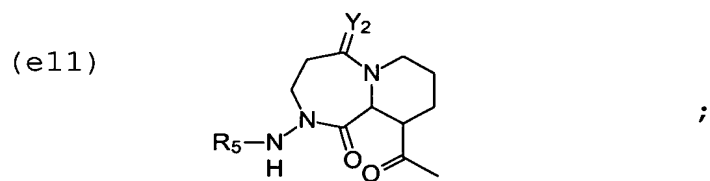
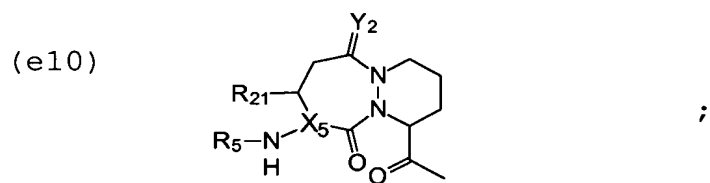
56. (previously presented) The method  
10 according to claim 55, wherein the disease is selected  
from the group consisting of osteoarthritis, acute  
pancreatitis, rheumatoid arthritis, inflammatory bowel  
disease, Crohn's disease, psoriasis, and Alzheimer's  
disease.

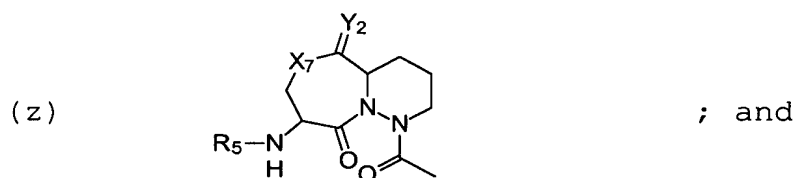
15 57. (previously presented) A compound  
represented by the formula:



20 wherein:

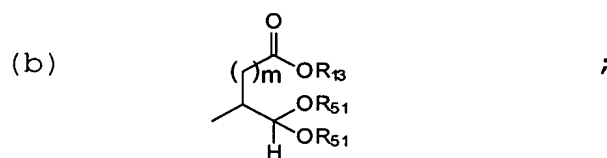
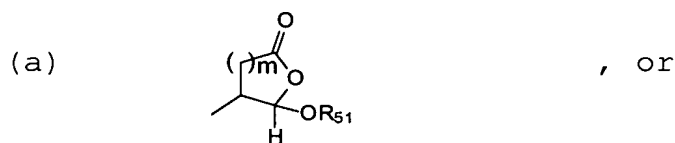
R<sub>1</sub> is selected from the group consisting of the  
following formulae:





ring C is chosen from the group consisting of  
 benzo, pyrido, thieno, pyrrolo, furano, thiazolo,  
 5 isothiazolo, oxazolo, isoxazolo, pyrimido, imidazolo,  
 cyclopentyl, and cyclohexyl;

R<sub>2</sub> is:



10 m is 1 or 2;

each R<sub>5</sub> is independently selected from the group  
 consisting of:

- 15
- C(O)-R<sub>10</sub>,
  - C(O)O-R<sub>9</sub>,
  - C(O)-N(R<sub>10</sub>)(R<sub>10</sub>)
  - S(O)<sub>2</sub>-R<sub>9</sub>,
  - S(O)<sub>2</sub>-NH-R<sub>10</sub>,
  - C(O)-CH<sub>2</sub>-O-R<sub>9</sub>,

-C(O)C(O)-R<sub>10</sub>,  
-R<sub>9</sub>,  
-H,  
-C(O)C(O)-OR<sub>10</sub>, and  
5 -C(O)C(O)-N(R<sub>9</sub>)(R<sub>10</sub>);

X<sub>5</sub> is CH or N;

Y<sub>2</sub> is H<sub>2</sub> or O;

10 X<sub>7</sub> is -N(R<sub>8</sub>)- or -O-;

R<sub>6</sub> is selected from the group consisting of -H and  
-CH<sub>3</sub>;

R<sub>8</sub> is selected from the group consisting of:  
15 -C(O)-R<sub>10</sub>,  
-C(O)O-R<sub>9</sub>,  
-C(O)-N(H)-R<sub>10</sub>,  
-S(O)<sub>2</sub>-R<sub>9</sub>,  
-S(O)<sub>2</sub>-NH-R<sub>10</sub>,  
20 -C(O)-CH<sub>2</sub>-OR<sub>10</sub>,  
-C(O)C(O)-R<sub>10</sub>;  
-C(O)-CH<sub>2</sub>N(R<sub>10</sub>)(R<sub>10</sub>),  
-C(O)-CH<sub>2</sub>C(O)-O-R<sub>9</sub>,  
-C(O)-CH<sub>2</sub>C(O)-R<sub>9</sub>,  
25 -H, and  
-C(O)-C(O)-OR<sub>10</sub>;

each R<sub>9</sub> is independently selected from the group  
consisting of -Ar<sub>3</sub> and a -C<sub>1-6</sub> straight or branched  
alkyl group optionally substituted with -Ar<sub>3</sub>, wherein  
30 the -C<sub>1-6</sub> alkyl group is optionally unsaturated;

each  $R_{10}$  is independently selected from the group consisting of -H, -Ar<sub>3</sub>, a -C<sub>3-6</sub> cycloalkyl group, and a -C<sub>1-6</sub> straight or branched alkyl group optionally substituted with -Ar<sub>3</sub>, wherein the -C<sub>1-6</sub> alkyl group is  
5 optionally unsaturated;

$R_{13}$  is selected from the group consisting of H, Ar<sub>3</sub>, and a -C<sub>1-6</sub> straight or branched alkyl group optionally substituted with -Ar<sub>3</sub>, -CONH<sub>2</sub>, -OR<sub>5</sub>, -OH, -OR<sub>9</sub>, or -CO<sub>2</sub>H;

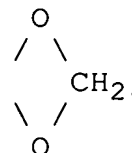
10 each  $R_{51}$  is independently selected from the group consisting of R<sub>9</sub>, -C(O)-R<sub>9</sub>, -C(O)-N(H)-R<sub>9</sub>, or each  $R_{51}$  taken together forms a saturated 4-8 member carbocyclic ring or heterocyclic ring containing -O-, -S-, or -NH-;

each  $R_{21}$  is independently selected from the group  
15 consisting of -H or a -C<sub>1-6</sub> straight or branched alkyl group;

each Ar<sub>3</sub> is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings  
20 and an aromatic heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO<sub>2</sub>, =N-, and -NH-, said heterocycle group optionally containing one or  
25 more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -Q<sub>1</sub>;

each  $Q_1$  is independently selected from the group consisting of  $-NH_2$ ,  $-CO_2H$ ,  $-Cl$ ,  $-F$ ,  $-Br$ ,  $-I$ ,  $-NO_2$ ,  $-CN$ ,  $=O$ ,  $-OH$ ,  $-perfluoro\ C_{1-3}\ alkyl$ ,  $R_5$ ,  $-OR_5$ ,  $-NHR_5$ ,  $-OR_9$ ,  $-N(R_9)(R_{10})$ ,  $-R_9$ ,  $-C(O)-R_{10}$ , and

5



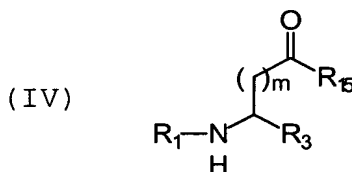
10

provided that when  $-Ar_3$  is substituted with a  $Q_1$  group which comprises one or more additional  $-Ar_3$  groups, said additional  $-Ar_3$  groups are not substituted with another  $-Ar_3$ .

58-61. (canceled)

15

62. (previously presented) A compound represented by the formula:



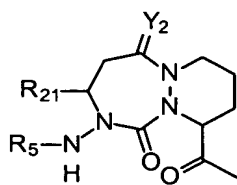
wherein:

$m$  is 1 or 2;

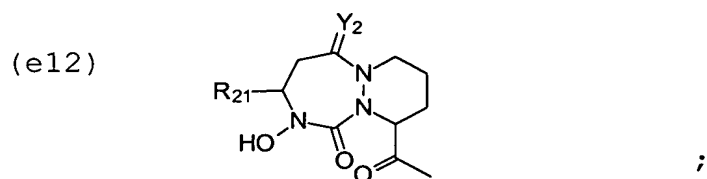
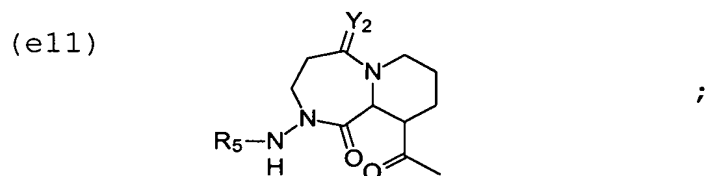
20

$R_1$  is selected from the group consisting of the following formulae:

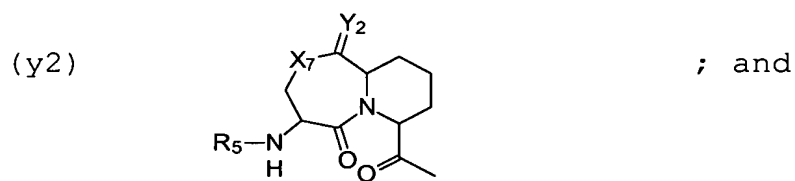
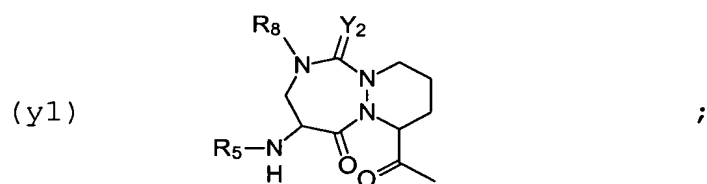
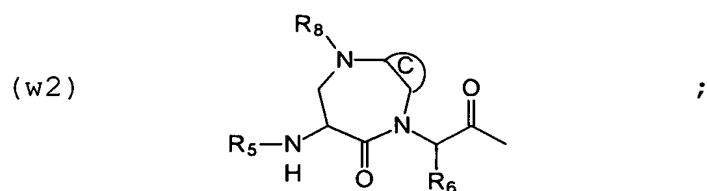
(e10-A)



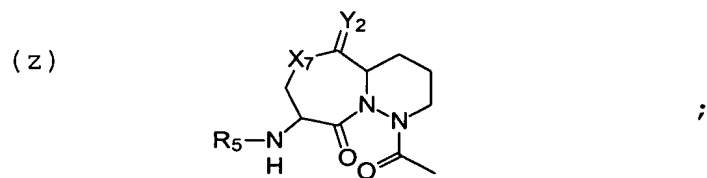
;



5



10



ring C is chosen from the group consisting of  
 15 benzo, pyrido, thieno, pyrrolo, furano, thiazolo,

isothiazolo, oxazolo, isoxazolo, pyrimido, imidazolo,  
cyclopentyl, and cyclohexyl;

R<sub>3</sub> is selected from the group consisting of:

- CN,
- 5        -C(O)-H,
- C(O)-CH<sub>2</sub>-T<sub>1</sub>-R<sub>11</sub>,
- C(O)-CH<sub>2</sub>-F,
- C=N-O-R<sub>9</sub>, and
- CO-Ar<sub>2</sub>;

10        each R<sub>5</sub> is independently selected from the group  
consisting of:

- C(O)-R<sub>10</sub>,
- C(O)O-R<sub>9</sub>,
- C(O)-N(R<sub>10</sub>)(R<sub>10</sub>)
- 15        -S(O)<sub>2</sub>-R<sub>9</sub>,
- S(O)<sub>2</sub>-NH-R<sub>10</sub>,
- C(O)-CH<sub>2</sub>-O-R<sub>9</sub>,
- C(O)C(O)-R<sub>10</sub>,
- R<sub>9</sub>,
- 20        -H,
- C(O)C(O)-OR<sub>10</sub>, and
- C(O)C(O)-N(R<sub>9</sub>)(R<sub>10</sub>);

Y<sub>2</sub> is H<sub>2</sub> or O;

25        X<sub>7</sub> is -N(R<sub>8</sub>)- or -O-;

each T<sub>1</sub> is independently selected from the group  
consisting of -O-, -S-, -S(O)-, and -S(O)<sub>2</sub>-;

R<sub>6</sub> is selected from the group consisting of -H and



-CH<sub>3</sub>;

R<sub>8</sub> is selected from the group consisting of:

-C(O)-R<sub>10</sub>,  
-C(O)O-R<sub>9</sub>,  
5 -C(O)-NH-R<sub>10</sub>,  
-S(O)<sub>2</sub>-R<sub>9</sub>,  
-S(O)<sub>2</sub>-NH-R<sub>10</sub>,  
-C(O)-CH<sub>2</sub>-OR<sub>10</sub>,  
-C(O)C(O)-R<sub>10</sub>,  
10 -C(O)-CH<sub>2</sub>-N(R<sub>10</sub>)(R<sub>10</sub>),  
-C(O)-CH<sub>2</sub>C(O)-O-R<sub>9</sub>,  
-C(O)-CH<sub>2</sub>C(O)-R<sub>9</sub>,  
-H, and  
-C(O)-C(O)-OR<sub>10</sub>;

15 each R<sub>9</sub> is independently selected from the group consisting of -Ar<sub>3</sub> and a -C<sub>1-6</sub> straight or branched alkyl group optionally substituted with -Ar<sub>3</sub>, wherein the -C<sub>1-6</sub> alkyl group is optionally unsaturated;

20 each R<sub>10</sub> is independently selected from the group consisting of -H, -Ar<sub>3</sub>, a -C<sub>3-6</sub> cycloalkyl group, and a -C<sub>1-6</sub> straight or branched alkyl group optionally substituted with -Ar<sub>3</sub>, wherein the -C<sub>1-6</sub> alkyl group is optionally unsaturated;

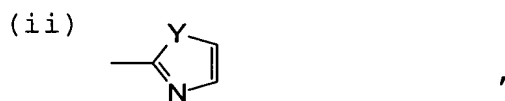
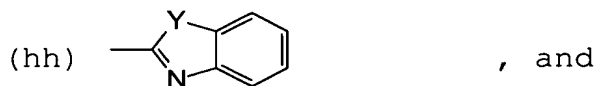
25 each R<sub>11</sub> is independently selected from the group consisting of:

-Ar<sub>4</sub>,  
-(CH<sub>2</sub>)<sub>1-3</sub>-Ar<sub>4</sub>,  
-H, and  
-C(O)-Ar<sub>4</sub>;

R<sub>15</sub> is selected from the group consisting of -OH, -OAr<sub>3</sub>, -N(H)-OH, and -OC<sub>1-6</sub>, wherein C<sub>1-6</sub> is a straight or branched alkyl group optionally substituted with -Ar<sub>3</sub>, -CONH<sub>2</sub>, -OR<sub>5</sub>, -OH, -OR<sub>9</sub>, or -CO<sub>2</sub>H;

5        each R<sub>21</sub> is independently selected from the group consisting of -H or a -C<sub>1-6</sub> straight or branched alkyl group;

Ar<sub>2</sub> is independently selected from the following group, in which any ring may optionally be singly or  
10       multiply substituted by -Q<sub>1</sub> or phenyl, optionally substituted by Q<sub>1</sub>:



15        wherein each Y is independently selected from the group consisting of O and S;

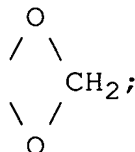
each Ar<sub>3</sub> is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings  
20       and an aromatic heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO<sub>2</sub>, =N-, and -NH-,  
-N(R<sub>5</sub>)-, and -N(R<sub>9</sub>)- said heterocycle group optionally  
25       containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings,

and said cyclic group optionally being singly or multiply substituted by -Q<sub>1</sub>;

each Ar<sub>4</sub> is a cyclic group independently selected from the set consisting of an aryl group which contains  
5 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO<sub>2</sub>, =N-, -NH-,  
10 -N(R<sub>5</sub>)-, and -N(R<sub>9</sub>)- said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -Q<sub>1</sub>;

15 each Q<sub>1</sub> is independently selected from the group consisting of -NH<sub>2</sub>, -CO<sub>2</sub>H, -Cl, -F, -Br, -I, -NO<sub>2</sub>, -CN, =O, -OH, -perfluoro C<sub>1-3</sub> alkyl, R<sub>5</sub>, -OR<sub>5</sub>, -NHR<sub>5</sub>, -OR<sub>9</sub>, -N(R<sub>9</sub>)(R<sub>10</sub>), -R<sub>9</sub>, -C(O)-R<sub>10</sub>, and

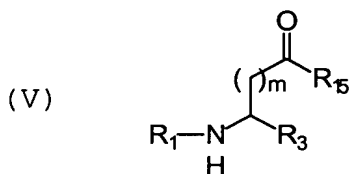
20



provided that when -Ar<sub>3</sub> is substituted with a Q<sub>1</sub> group which comprises one or more additional -Ar<sub>3</sub>  
25 groups, said additional -Ar<sub>3</sub> groups are not substituted with another -Ar<sub>3</sub>.

63-65. (canceled)

30 66. (previously presented) A compound represented by the formula:

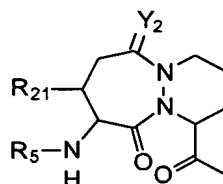


wherein:

m is 1 or 2;

5 R<sub>1</sub> is:

(e10-B)



;

R<sub>3</sub> is selected from the group consisting of:

- CN,
- C(O)-H,
- C(O)-CH<sub>2</sub>-T<sub>1</sub>-R<sub>11</sub>,
- C(O)-CH<sub>2</sub>-F,
- C=N-O-R<sub>9</sub>, and
- CO-Ar<sub>2</sub>;

15 each R<sub>5</sub> is -C(O)C(O)-OR<sub>10</sub>;

Y<sub>2</sub> is H<sub>2</sub> or O;

each T<sub>1</sub> is independently selected from the group consisting of -O-, -S-, -S(O)-, and -S(O)<sub>2</sub>-;

20 each R<sub>9</sub> is independently selected from the group consisting of -Ar<sub>3</sub> and a -C<sub>1-6</sub> straight or branched alkyl group optionally substituted with -Ar<sub>3</sub>, wherein the -C<sub>1-6</sub> alkyl group is optionally unsaturated;

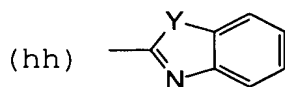
each  $R_{10}$  is independently selected from the group consisting of -H, -Ar<sub>3</sub>, a -C<sub>3-6</sub> cycloalkyl group, and a -C<sub>1-6</sub> straight or branched alkyl group optionally substituted with -Ar<sub>3</sub>, wherein the -C<sub>1-6</sub> alkyl group is  
5 optionally unsaturated;

each  $R_{11}$  is independently selected from the group consisting of:  
-Ar<sub>4</sub>,  
-(CH<sub>2</sub>)<sub>1-3</sub>-Ar<sub>4</sub>,  
10 -H, and  
-C(O)-Ar<sub>4</sub>;

$R_{15}$  is selected from the group consisting of -OH, -OAr<sub>3</sub>, -N(H)-OH, and -OC<sub>1-6</sub>, wherein C<sub>1-6</sub> is a straight or branched alkyl group optionally substituted with  
15 -Ar<sub>3</sub>, -CONH<sub>2</sub>, -OR<sub>5</sub>, -OH, -OR<sub>9</sub>, or -CO<sub>2</sub>H;

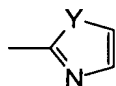
each  $R_{21}$  is independently selected from the group consisting of -H or a -C<sub>1-6</sub> straight or branched alkyl group;

Ar<sub>2</sub> is independently selected from the following  
20 group, in which any ring may optionally be singly or multiply substituted by -Q<sub>1</sub> or phenyl, optionally substituted by Q<sub>1</sub>:



, and

(ii)



wherein each Y is independently selected from the group consisting of O and S;

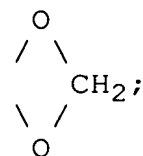
5           each Ar<sub>3</sub> is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings and an aromatic heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said  
10   heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO<sub>2</sub>, =N-, and -NH-, -N(R<sub>5</sub>)-, and -N(R<sub>9</sub>)- said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings,  
15   and said cyclic group optionally being singly or multiply substituted by -Q<sub>1</sub>;

          each Ar<sub>4</sub> is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3  
20   rings, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO<sub>2</sub>, =N-, -NH-, -N(R<sub>5</sub>)-, and -N(R<sub>9</sub>)- said heterocycle group optionally  
25   containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -Q<sub>1</sub>;

each Q<sub>1</sub> is independently selected from the group

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Supp. Amdt. dated March 11, 2004

consisting of  $-\text{NH}_2$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{Cl}$ ,  $-\text{F}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{NO}_2$ ,  $-\text{CN}$ ,  
 $=\text{O}$ ,  $-\text{OH}$ ,  $-\text{perfluoro C}_{1-3}$  alkyl,  $\text{R}_5$ ,  $-\text{OR}_5$ ,  $-\text{NHR}_5$ ,  $-\text{OR}_9$ ,  
 $-\text{N}(\text{R}_9)(\text{R}_{10})$ ,  $-\text{R}_9$ ,  $-\text{C}(\text{O})-\text{R}_{10}$ , and



5

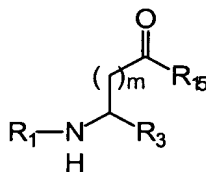
provided that when  $-\text{Ar}_3$  is substituted with a  $\text{Q}_1$   
group which comprises one or more additional  $-\text{Ar}_3$   
10 groups, said additional  $-\text{Ar}_3$  groups are not substituted  
with another  $-\text{Ar}_3$ .

67. (canceled)

68. (previously presented) A compound  
represented by the formula:

15

(V)



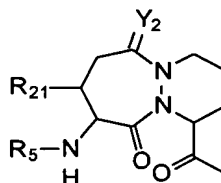
wherein:

$m$  is 1 or 2;

$\text{R}_1$  is:

20

(e10-B)



;

$\text{R}_3$  is selected from the group consisting of:  
 $-\text{CN}$ ,

5                   -C(O)-H,  
                  -C(O)-CH<sub>2</sub>-T<sub>1</sub>-R<sub>11</sub>,  
                  -C(O)-CH<sub>2</sub>-F,  
                  -C=N-O-R<sub>9</sub>, and  
                  -CO-Ar<sub>2</sub>;

each R<sub>5</sub> is independently selected from the group  
consisting of:

10                   -C(O)-R<sub>10</sub>,  
                  -C(O)O-R<sub>9</sub>,  
                  -C(O)-N(R<sub>10</sub>)(R<sub>10</sub>)  
                  -S(O)<sub>2</sub>-R<sub>9</sub>,  
                  -S(O)<sub>2</sub>-NH-R<sub>10</sub>,  
                  -C(O)-CH<sub>2</sub>-O-R<sub>9</sub>,  
                  -C(O)C(O)-R<sub>10</sub>,  
15                   -R<sub>9</sub>,  
                  -H,  
                  -C(O)C(O)-OR<sub>10</sub>, and  
                  -C(O)C(O)-N(R<sub>9</sub>)(R<sub>10</sub>);

20                   Y<sub>2</sub> is H<sub>2</sub> or O;

each T<sub>1</sub> is independently selected from the group  
consisting of -O-, -S-, -S(O)-, and -S(O)<sub>2</sub>-;

25                   each R<sub>9</sub> is independently selected from the group  
consisting of -Ar<sub>3</sub> and a -C<sub>1-6</sub> straight or branched  
alkyl group optionally substituted with -Ar<sub>3</sub>, wherein  
the -C<sub>1-6</sub> alkyl group is optionally unsaturated;

30                   each R<sub>10</sub> is independently selected from the group  
consisting of -H, -Ar<sub>3</sub>, a -C<sub>3-6</sub> cycloalkyl group, and a  
-C<sub>1-6</sub> straight or branched alkyl group optionally



substituted with  $-\text{Ar}_3$ , wherein the  $-\text{C}_{1-6}$  alkyl group is optionally unsaturated;

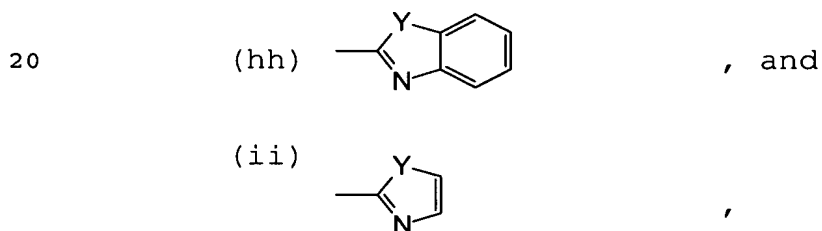
each  $\text{R}_{11}$  is independently selected from the group consisting of:

- 5            $-\text{Ar}_4$ ,  
             $-(\text{CH}_2)_{1-3}-\text{Ar}_4$ ,  
             $-\text{H}$ , and  
             $-\text{C}(\text{O})-\text{Ar}_4$ ;

10            $\text{R}_{15}$  is selected from the group consisting of  $-\text{OH}$ ,  
             $-\text{OAr}_3$ ,  $-\text{N}(\text{H})-\text{OH}$ , and  $-\text{OC}_{1-6}$ , wherein  $\text{C}_{1-6}$  is a straight  
            or branched alkyl group optionally substituted with  
             $-\text{Ar}_3$ ,  $-\text{CONH}_2$ ,  $-\text{OR}_5$ ,  $-\text{OH}$ ,  $-\text{OR}_9$ , or  $-\text{CO}_2\text{H}$ ;

15           each  $\text{R}_{21}$  is independently selected from the group  
            consisting of  $-\text{H}$  or a  $-\text{C}_{1-6}$  straight or branched alkyl  
            group;

$\text{Ar}_2$  is independently selected from the following  
            group, in which any ring may optionally be singly or  
            multiply substituted by  $-\text{Q}_1$  or phenyl, optionally  
            substituted by  $\text{Q}_1$ :

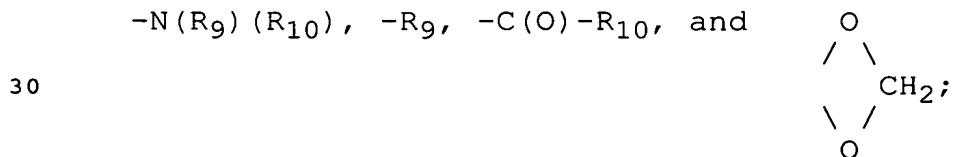


            wherein each  $\text{Y}$  is independently selected from the  
            group consisting of  $\text{O}$  and  $\text{S}$ ;

each Ar<sub>3</sub> is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings and an aromatic heterocycle group containing between 5  
5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO<sub>2</sub>, =N-, and -NH-, -N(R<sub>5</sub>)-, and -N(R<sub>9</sub>)- said heterocycle group optionally containing one or more double bonds, said heterocycle  
10 group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -Q<sub>1</sub>;

each Ar<sub>4</sub> is a cyclic group independently selected from the set consisting of an aryl group which contains  
15 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from -O-, -S-, -SO-, SO<sub>2</sub>, =N-, -NH-,  
20 -N(R<sub>5</sub>)-, and -N(R<sub>9</sub>)- said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -Q<sub>1</sub>;

25 each Q<sub>1</sub> is independently selected from the group consisting of -NH<sub>2</sub>, -CO<sub>2</sub>H, -Cl, -F, -Br, -I, -NO<sub>2</sub>, -CN, =O, -OH, -perfluoro C<sub>1-3</sub> alkyl, R<sub>5</sub>, -OR<sub>5</sub>, -NHR<sub>5</sub>, -OR<sub>9</sub>, -N(R<sub>9</sub>)(R<sub>10</sub>), -R<sub>9</sub>, -C(O)-R<sub>10</sub>, and



provided that when  $-\text{Ar}_3$  is substituted with a  $\text{Q}_1$  group which comprises one or more additional  $-\text{Ar}_3$  groups, said additional  $-\text{Ar}_3$  groups are not substituted with another  $-\text{Ar}_3$ ;

5           provided that when:

m is 1;

$\text{R}_{15}$  is  $-\text{OH}$ ;

$\text{R}_{21}$  is  $-\text{H}$ ; and

$\text{Y}_2$  is O and  $\text{R}_3$  is  $-\text{C}(\text{O})-\text{H}$ , then  $\text{R}_5$  cannot be:  
10            $-\text{C}(\text{O})-\text{R}_{10}$ , wherein  $\text{R}_{10}$  is  $-\text{Ar}_3$  and the  $\text{Ar}_3$  cyclic group is phenyl, unsubstituted by  $-\text{Q}_1$ , 4-(carboxymethoxy)phenyl, 2-fluorophenyl, 2-pyridyl, N-(4-methylpiperazino)methylphenyl, or  
               $-\text{C}(\text{O})-\text{OR}_9$ , wherein  $\text{R}_9$  is  $-\text{CH}_2-\text{Ar}_3$ , and the  $\text{Ar}_3$   
15           cyclic group is phenyl, unsubstituted by  $-\text{Q}_1$ ; and when

$\text{Y}_2$  is O,  $\text{R}_3$  is  $-\text{C}(\text{O})-\text{CH}_2-\text{T}_1-\text{R}_{11}$ ,  $\text{T}_1$  is O, and  $\text{R}_{11}$  is  $\text{Ar}_4$ , wherein the  $\text{Ar}_4$  cyclic group is 5-(1-(4-chlorophenyl)-3-trifluoromethyl)pyrazolyl), then  $\text{R}_5$  cannot be:

20            $-\text{H}$ ;

$-\text{C}(\text{O})-\text{R}_{10}$ , wherein  $\text{R}_{10}$  is  $-\text{Ar}_3$  and the  $\text{Ar}_3$  cyclic group is 4-(dimethylaminomethyl)phenyl, phenyl, 4-(carboxymethylthio)phenyl, 4-(carboxyethylthio)phenyl, 4-(carboxyethyl)phenyl, 4-(carboxypropyl)phenyl, 2-fluorophenyl, 2-pyridyl, N-(4-methylpiperazino)methylphenyl, or

25            $-\text{C}(\text{O})-\text{OR}_9$ , wherein  $\text{R}_9$  is isobutyl or  $-\text{CH}_2-\text{Ar}_3$  and the  $\text{Ar}_3$  cyclic group is phenyl;

              and when  $\text{R}_{11}$  is  $\text{Ar}_4$ , wherein the  $\text{Ar}_4$  cyclic group

is 5-(1-phenyl-3-trifluoromethyl)pyrazolyl or 5-(1-(4-chloro-2-pyridinyl)-3-trifluoromethyl)pyrazolyl, then  $R_5$  cannot be:

5         $-C(O)-OR_9$ , wherein  $R_9$  is  $-CH_2-Ar_3$ , and the  $Ar_3$  cyclic group is phenyl;

and when  $R_{11}$  is  $Ar_4$ , wherein the  $Ar_4$  cyclic group is 5-(1-(2-pyridyl)-3-trifluoromethyl)pyrazolyl), then  $R_5$  cannot be:

10         $-C(O)-R_{10}$ , wherein  $R_{10}$  is  $-Ar_3$  and the  $Ar_3$  cyclic group is 4-(dimethylaminomethyl)phenyl, or

$-C(O)-OR_9$ , wherein  $R_9$  is  $-CH_2-Ar_3$ , and the  $Ar_3$  cyclic group is phenyl, unsubstituted by  $-Q_1$ ; and when

15         $Y_2$  is O,  $R_3$  is  $-C(O)-CH_2-T_1-R_{11}$ ,  $T_1$  is O, and  $R_{11}$  is  $-C(O)-Ar_4$ , wherein the  $Ar_4$  cyclic group is 2,5-dichlorophenyl, then  $R_5$  cannot be:

$-C(O)-R_{10}$ , wherein  $R_{10}$  is  $-Ar_3$  and the  $Ar_3$  cyclic group is 4-(dimethylaminomethyl)phenyl, 4-(N-morpholinomethyl)phenyl, 4-(N-methylpiperazino)methyl)phenyl, 4-(N-(2-methyl)imidazolylmethyl)phenyl, 5-benzimidazolyl, 5-benzotriazolyl, N-carboethoxy-5-benzotriazolyl, N-carboethoxy-5-benzimidazolyl, or

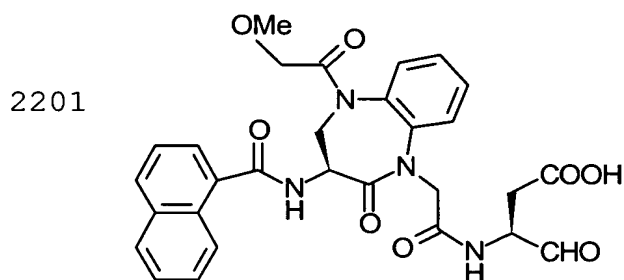
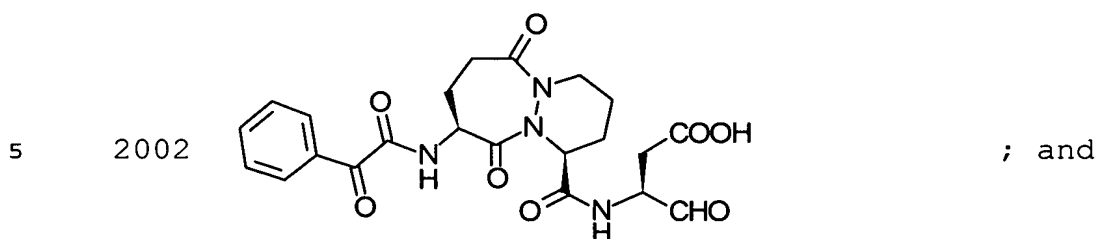
$-C(O)-OR_9$ , wherein  $R_9$  is  $-CH_2-Ar_3$ , and the  $Ar_3$  cyclic group is phenyl, unsubstituted by  $-Q_1$ ; and when

25         $Y_2$  is  $H_2$ ,  $R_3$  is  $-C(O)-CH_2-T_1-R_{11}$ ,  $T_1$  is O, and  $R_{11}$  is  $-C(O)-Ar_4$ , wherein the  $Ar_4$  cyclic group is 2,5-dichlorophenyl, then  $R_5$  cannot be:

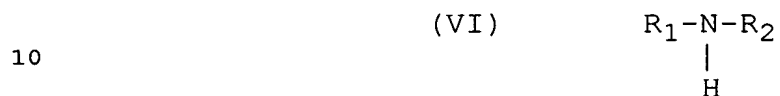
$-C(O)-OR_9$ , wherein  $R_9$  is  $-CH_2-Ar_3$  and the  $Ar_3$  cyclic group is phenyl.

69-78. (canceled)

79. (previously presented) The compound according to claim 68, selected from the group consisting of:

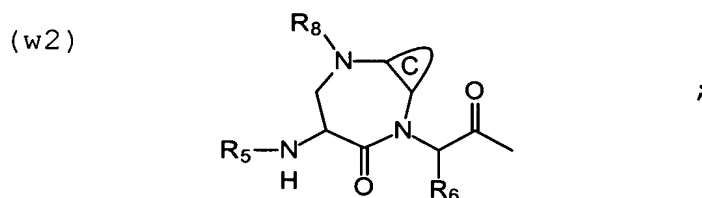
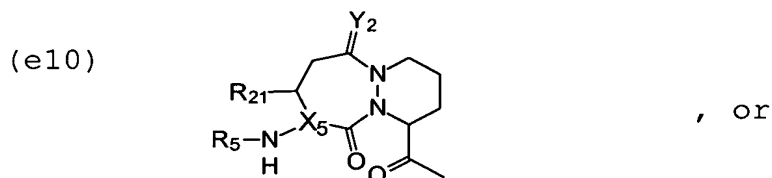


80. (previously presented) A compound represented by the formula:



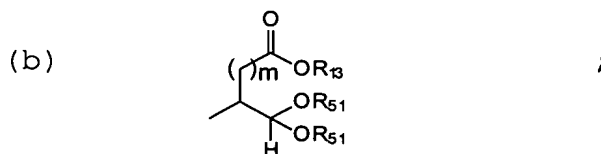
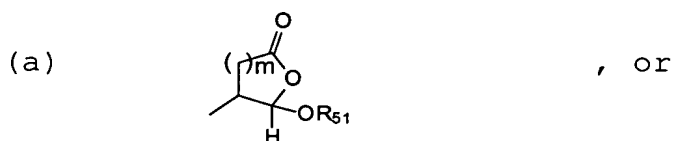
wherein:

$R_1$  is:



5 C is a ring chosen from the set consisting of benzo, pyrido, thieno, pyrrolo, furano, thiazolo, isothiazolo, oxazolo, isoxazolo, pyrimido, imidazolo, cyclopentyl, and cyclohexyl; the ring optionally being singly or multiply substituted by -Q<sub>1</sub>;

10 R<sub>2</sub> is:



m is 1 or 2;

15 each R<sub>5</sub> is independently selected from the group consisting of:

- C(O)-R<sub>10</sub>,
- C(O)O-R<sub>9</sub>,

5                   -C(O)-N(R<sub>10</sub>)(R<sub>10</sub>)  
                  -S(O)<sub>2</sub>-R<sub>9</sub>,  
                  -S(O)<sub>2</sub>-NH-R<sub>10</sub>,  
                  -C(O)-CH<sub>2</sub>-O-R<sub>9</sub>,  
                  -C(O)C(O)-R<sub>10</sub>,  
                  -R<sub>9</sub>,  
                  -H,  
                  -C(O)C(O)-OR<sub>10</sub>, and  
                  -C(O)C(O)-N(R<sub>9</sub>)(R<sub>10</sub>);

10               X<sub>5</sub> is CH or N;

                  Y<sub>2</sub> is H<sub>2</sub> or O;

15               R<sub>6</sub> is selected from the group consisting of -H and  
                  -CH<sub>3</sub>;

                  R<sub>8</sub> is selected from the group consisting of:

                  -C(O)-R<sub>10</sub>,  
                  -C(O)O-R<sub>9</sub>,  
20               -C(O)-N(H)-R<sub>10</sub>,  
                  -S(O)<sub>2</sub>-R<sub>9</sub>,  
                  -S(O)<sub>2</sub>-NH-R<sub>10</sub>,  
                  -C(O)-CH<sub>2</sub>-OR<sub>10</sub>,  
                  -C(O)C(O)-R<sub>10</sub>;  
25               -C(O)-CH<sub>2</sub>N(R<sub>10</sub>)(R<sub>10</sub>),  
                  -C(O)-CH<sub>2</sub>C(O)-O-R<sub>9</sub>,  
                  -C(O)-CH<sub>2</sub>C(O)-R<sub>9</sub>,  
                  -H, and  
                  -C(O)-C(O)-OR<sub>10</sub>;

30               each R<sub>9</sub> is independently selected from the group  
                  consisting of -Ar<sub>3</sub> and a -C<sub>1-6</sub> straight or branched

alkyl group optionally substituted with -Ar<sub>3</sub>, wherein  
the -C<sub>1-6</sub> alkyl group is optionally unsaturated;

each R<sub>10</sub> is independently selected from the group  
consisting of -H, -Ar<sub>3</sub>, a -C<sub>3-6</sub> cycloalkyl group, and a  
5 -C<sub>1-6</sub> straight or branched alkyl group optionally  
substituted with -Ar<sub>3</sub>, wherein the -C<sub>1-6</sub> alkyl group is  
optionally unsaturated;

R<sub>13</sub> is selected from the group consisting of H,  
Ar<sub>3</sub>, and a -C<sub>1-6</sub> straight or branched alkyl group  
10 optionally substituted with -Ar<sub>3</sub>, -CONH<sub>2</sub>, -OR<sub>5</sub>, -OH,  
-OR<sub>9</sub>, or -CO<sub>2</sub>H;

each R<sub>51</sub> is independently selected from the group  
consisting of R<sub>9</sub>, -C(O)-R<sub>9</sub>, -C(O)-N(H)-R<sub>9</sub>, or each R<sub>51</sub>  
taken together forms a saturated 4-8 member carbocyclic  
15 ring or heterocyclic ring containing -O-, -S-, or -NH-;

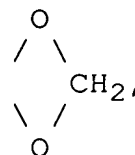
each R<sub>21</sub> is independently selected from the group  
consisting of -H or a -C<sub>1-6</sub> straight or branched alkyl  
group;

each Ar<sub>3</sub> is a cyclic group independently selected  
20 from the set consisting of an aryl group which contains  
6, 10, 12, or 14 carbon atoms and between 1 and 3 rings  
and an aromatic heterocycle group containing between 5  
and 15 ring atoms and between 1 and 3 rings, said  
heterocyclic group containing at least one heteroatom  
25 group selected from -O-, -S-, -SO-, SO<sub>2</sub>, =N-, and -NH-,  
said heterocycle group optionally containing one or  
more double bonds, said heterocycle group optionally  
comprising one or more aromatic rings, and said cyclic



group optionally being singly or multiply substituted  
by  $-Q_1$ ;

each  $Q_1$  is independently selected from the group  
consisting of  $-\text{NH}_2$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{Cl}$ ,  $-\text{F}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{NO}_2$ ,  $-\text{CN}$ ,  
 $=\text{O}$ ,  $-\text{OH}$ , -perfluoro  $\text{C}_{1-3}$  alkyl,  $\text{R}_5$ ,  $-\text{OR}_5$ ,  $-\text{NHR}_5$ ,  $-\text{OR}_9$ ,  
 $-\text{N}(\text{R}_9)(\text{R}_{10})$ ,  $-\text{R}_9$ ,  $-\text{C}(\text{O})-\text{R}_{10}$ , and



provided that when  $-\text{Ar}_3$  is substituted with a  $Q_1$   
group which comprises one or more additional  $-\text{Ar}_3$   
groups, said additional  $-\text{Ar}_3$  groups are not substituted  
with another  $-\text{Ar}_3$ .

81. (previously presented) The compound  
according to claim 80, wherein:

$m$  is 1;

$\text{C}$  is a ring chosen from the set consisting of  
benzo, pyrido, or thieno the ring optionally being  
singly or multiply substituted by halogen,  $-\text{NH}_2$ ,  
 $-\text{NH}-\text{R}_5$ ,  $-\text{NH}-\text{R}_9$ ,  $-\text{OR}_{10}$ , or  $-\text{R}_9$ , wherein  $\text{R}_9$  is a straight  
or branched  $\text{C}_{1-4}$  alkyl group, and  $\text{R}_{10}$  is H or a straight  
or branched  $\text{C}_{1-4}$  alkyl group;

$\text{R}_6$  is H;

$\text{R}_{13}$  is H or a  $\text{C}_{1-4}$  straight or branched alkyl group  
optionally substituted with  $-\text{Ar}_3$ ,  $-\text{OH}$ ,  $-\text{OR}_9$ ,  $-\text{CO}_2\text{H}$ ,  
wherein the  $\text{R}_9$  is a  $\text{C}_{1-4}$  branched or straight chain  
alkyl group; wherein  $\text{Ar}_3$  is morpholinyl or phenyl,

wherein the phenyl is optionally substituted by -Q<sub>1</sub>;

R<sub>21</sub> is -H or -CH<sub>3</sub>;

R<sub>51</sub> is a C<sub>1-6</sub> straight or branched alkyl group  
optionally substituted with -Ar<sub>3</sub>, wherein Ar<sub>3</sub> is  
5 phenyl, optionally substituted by -Q<sub>1</sub>;

each Ar<sub>3</sub> cyclic group is independently selected  
from the set consisting of phenyl, naphthyl, thienyl,  
quinolinyl, isoquinolinyl, pyrazolyl, thiazolyl,  
isoxazolyl, benzotriazolyl, benzimidazolyl,  
10 thienothienyl, imidazolyl, thiadiazolyl,  
benzo[b]thiophenyl, pyridyl, benzofuranyl, and indolyl,  
and said cyclic group optionally being singly or  
multiply substituted by -Q<sub>1</sub>;

each Q<sub>1</sub> is independently selected from the group  
15 consisting of -NH<sub>2</sub>, -Cl, -F, -Br, -OH, -R<sub>9</sub>, -NH-R<sub>5</sub>  
wherein R<sub>5</sub> is -C(O)-R<sub>10</sub> or -S(O)<sub>2</sub>-R<sub>9</sub>, -OR<sub>5</sub> wherein R<sub>5</sub> is  
-C(O)-R<sub>10</sub>, -OR<sub>9</sub>, -NHR<sub>9</sub>, and

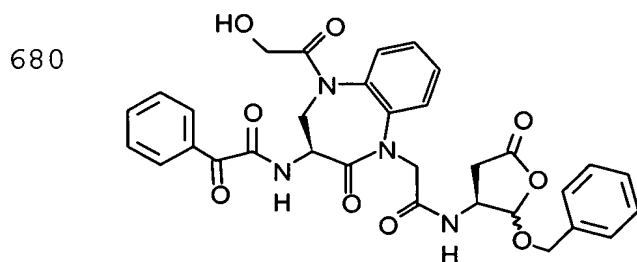
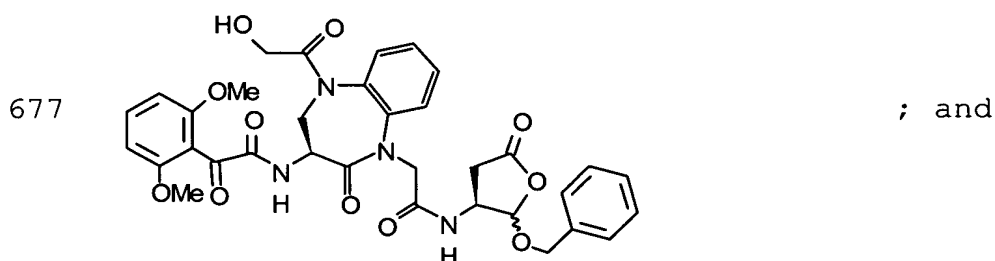


wherein each R<sub>9</sub> and R<sub>10</sub> are independently a -C<sub>1-6</sub>  
straight or branched alkyl group optionally substituted  
25 with -Ar<sub>3</sub> wherein Ar<sub>3</sub> is phenyl;

provided that when -Ar<sub>3</sub> is substituted with a Q<sub>1</sub>  
group which comprises one or more additional -Ar<sub>3</sub>  
groups, said additional -Ar<sub>3</sub> groups are not substituted  
30 with another -Ar<sub>3</sub>.

82. (previously presented) The compound according to claim 81, wherein  $R_1$  is (w2).

83. (previously presented) The compound according to claim 82, selected from the group consisting of:



84-87. (canceled)

88. (previously presented) The compound according to claim 80 wherein  $R_5$  is  $-C(O)-R_{10}$  or  $-C(O)-C(O)-R_{10}$ .

89. (previously presented) The compound according to claim 88, wherein  $R_{10}$  is  $Ar_3$ .

90. (previously presented) The compound according to claim 89, wherein:

$R_5$  is  $-C(O)-R_{10}$  and  $R_{10}$  is  $Ar_3$ , wherein the  $Ar_3$  cyclic group is phenyl optionally being singly or

multiply substituted by:

-R<sub>9</sub>, wherein R<sub>9</sub> is a C<sub>1-4</sub> straight or branched alkyl group;

-F,

5

-Cl,

-N(H)-R<sub>5</sub>, wherein -R<sub>5</sub> is -H or -C(O)-R<sub>10</sub>, wherein R<sub>10</sub> is a -C<sub>1-6</sub> straight or branched alkyl group optionally substituted with -Ar<sub>3</sub>, wherein Ar<sub>3</sub> is phenyl,

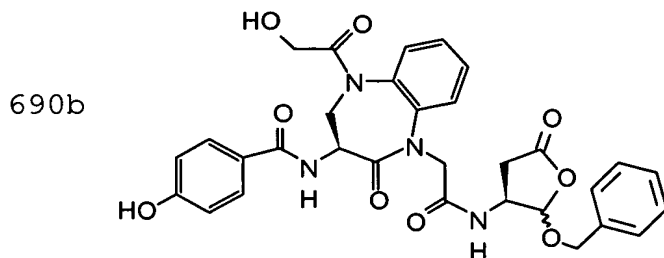
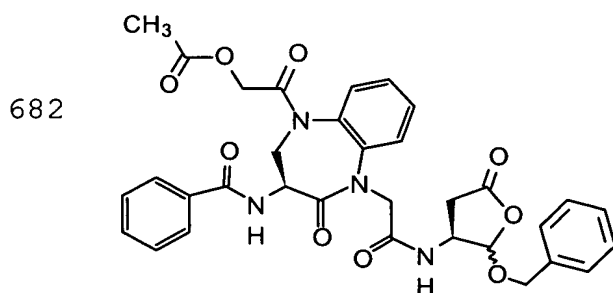
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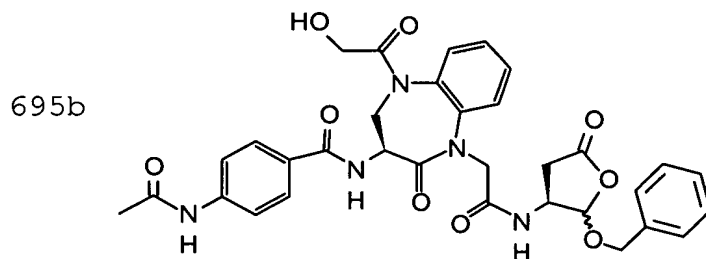
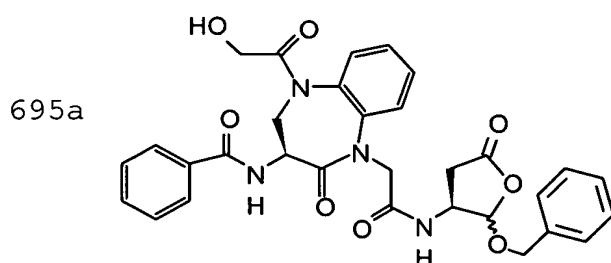
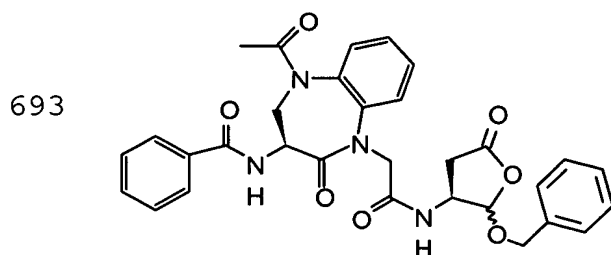
-N(R<sub>9</sub>)(R<sub>10</sub>), wherein R<sub>9</sub> and R<sub>10</sub> are independently a -C<sub>1-4</sub> straight or branched alkyl group, or

-O-R<sub>5</sub>, wherein R<sub>5</sub> is H or a -C<sub>1-4</sub> straight or branched alkyl group.

15

91. (previously presented) The compound according to claim 90, selected from the group consisting of:





92. (previously presented) The compound  
5 according to claim 90, wherein Ar<sub>3</sub> is phenyl being  
singly or multiply substituted at the 3- or 5-position  
by -Cl or at the 4-position by -NH-R<sub>5</sub>, -N(R<sub>9</sub>)(R<sub>10</sub>), or  
-O-R<sub>5</sub>.

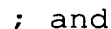
93. (previously presented) The compound  
10 according to claim 92, selected from the group  
consisting of:



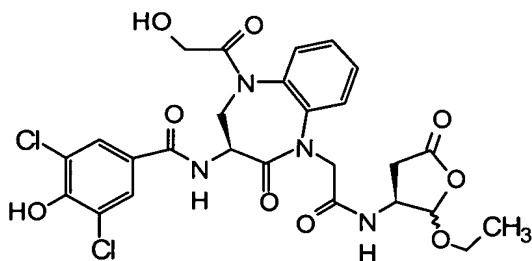
688a



692a



692b



5

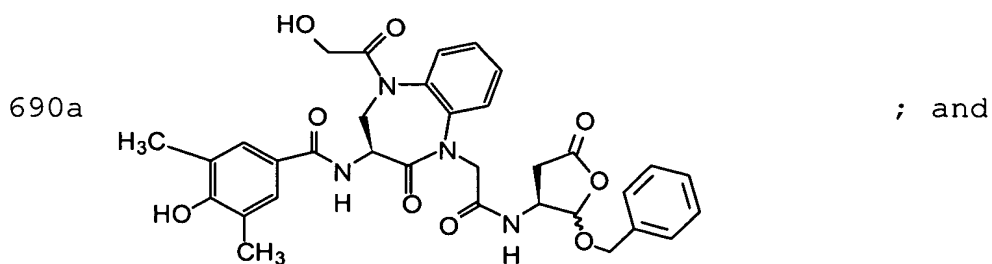
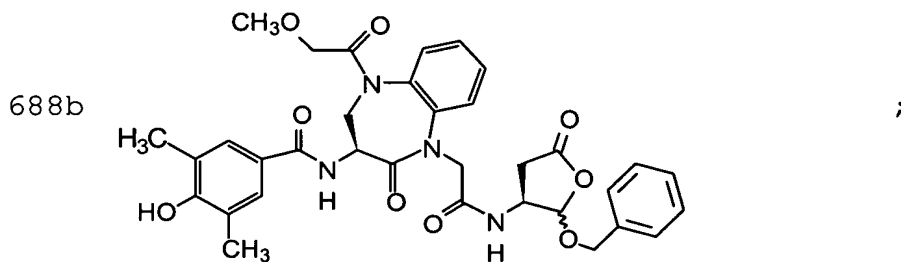
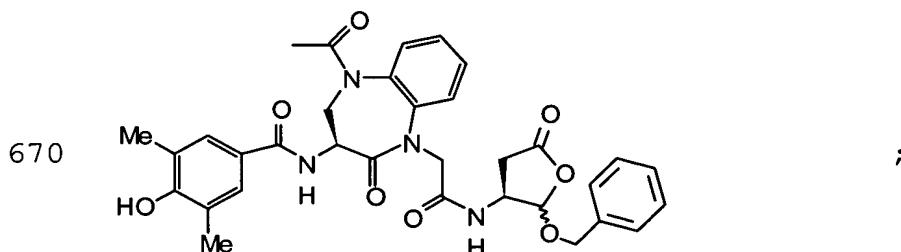
95. (previously presented) The compound to claim 90, wherein Ar<sub>3</sub> is phenyl being multiply substituted at the 3- or 5-position wherein R<sub>9</sub> is a C<sub>1-4</sub> straight or branched alkyl

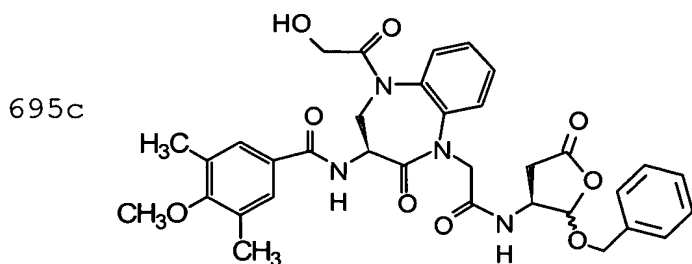
group;

and at the 4-position by -O-R<sub>5</sub>.

96. (previously presented) The compound  
according to claim 95, selected from the group  
consisting of:

5





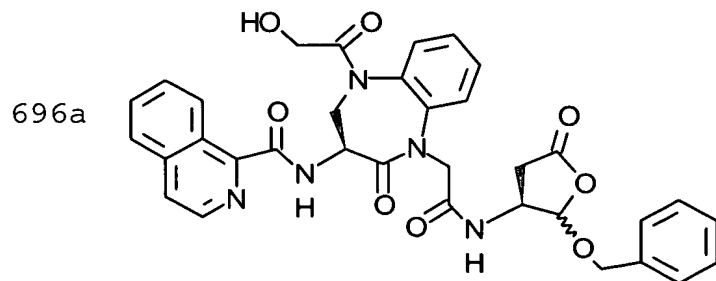
97. (canceled)

98. (previously presented) The compound according to claim 89, wherein:

5         $R_5$  is  $-C(O)-R_{10}$ , wherein  $R_{10}$  is  $Ar_3$  and the  $Ar_3$  cyclic group is selected from the group consisting of is indolyl, benzimidazolyl, thienyl, quinolyl, isoquinolyl and benzo[b]thiophenyl, and said cyclic group optionally being singly or multiply substituted  
10        by  $-Q_1$ .

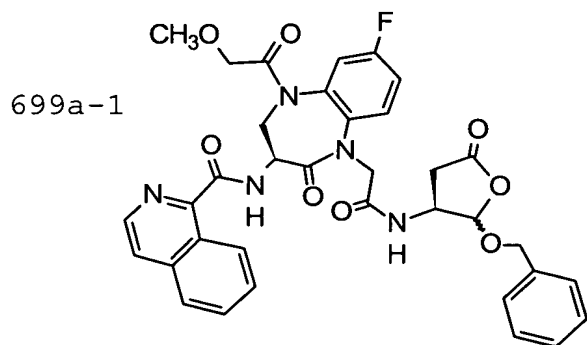
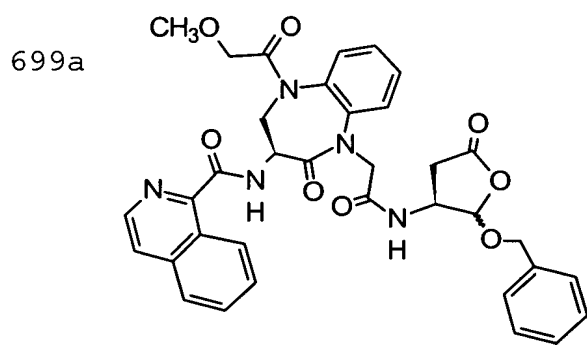
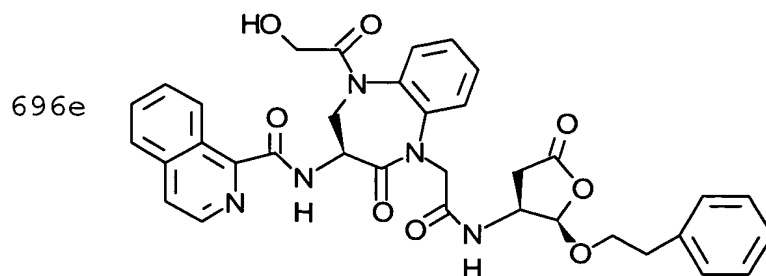
99. (previously presented) The compound according to claim 98, wherein the  $Ar_3$  cyclic group is isoquinolyl, and said cyclic group optionally being singly or multiply substituted by  $-Q_1$ .

15        100. (previously presented) The compound according to claim 99 selected from the group consisting of:







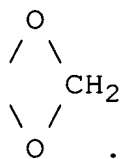


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101. (canceled)

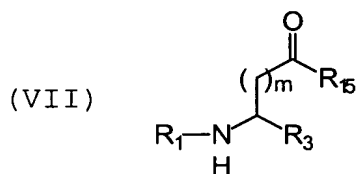
102. (previously presented) The compound according to claim 89, wherein  $R_5$  is  $-C(O)-R_{10}$ , wherein  $R_{10}$  is  $Ar_3$  and the  $Ar_3$  cyclic group is phenyl, substituted by

5



103. (canceled)

104. (previously presented) A compound represented by the formula:

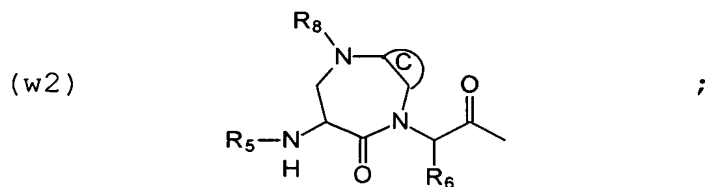


10 wherein:

m is 1 or 2;

R<sub>1</sub> is selected from the group consisting of the following formulae:

15



C is a ring chosen from the set consisting of benzo, pyrido, thieno, pyrrolo, furano, thiazolo, isothiazolo, oxazolo, isoxazolo, pyrimido, imidazolo, cyclopentyl, and cyclohexyl, the ring optionally being singly or multiply substituted by -Q<sub>1</sub>,;

R<sub>3</sub> is selected from the group consisting of:

5                   -CN,  
                  -C(O)-H,  
                  -C(O)-CH<sub>2</sub>-T<sub>1</sub>-R<sub>11</sub>,  
                  -C(O)-CH<sub>2</sub>-F,  
                  -C=N-O-R<sub>9</sub>, and  
                  -CO-Ar<sub>2</sub>;

each R<sub>5</sub> is independently selected from the group  
consisting of:

10                   -C(O)-R<sub>10</sub>,  
                  -C(O)O-R<sub>9</sub>,  
                  -C(O)-N(R<sub>10</sub>)(R<sub>10</sub>)  
                  -S(O)<sub>2</sub>-R<sub>9</sub>,  
                  -S(O)<sub>2</sub>-NH-R<sub>10</sub>,  
                  -C(O)-CH<sub>2</sub>-O-R<sub>9</sub>,  
15                   -C(O)C(O)-R<sub>10</sub>,  
                  -R<sub>9</sub>,  
                  -H,  
                  -C(O)C(O)-OR<sub>10</sub>, and  
                  -C(O)C(O)-N(R<sub>9</sub>)(R<sub>10</sub>);

20

each T<sub>1</sub> is independently selected from the group  
consisting of -O-, -S-, -S(O)-, and -S(O)<sub>2</sub>-;

25                   R<sub>6</sub> is selected from the group consisting of -H and  
                  -CH<sub>3</sub>;

R<sub>8</sub> is selected from the group consisting of:

30                   -C(O)-R<sub>10</sub>,  
                  -C(O)O-R<sub>9</sub>,  
                  -C(O)-NH-R<sub>10</sub>,  
                  -S(O)<sub>2</sub>-R<sub>9</sub>,  
                  -S(O)<sub>2</sub>-NH-R<sub>10</sub>,

5  
-C(O)-CH<sub>2</sub>-OR<sub>10</sub>,  
-C(O)C(O)-R<sub>10</sub>,  
-C(O)-CH<sub>2</sub>-N(R<sub>10</sub>)(R<sub>10</sub>),  
-C(O)-CH<sub>2</sub>C(O)-O-R<sub>9</sub>,  
-C(O)-CH<sub>2</sub>C(O)-R<sub>9</sub>,  
-H, and  
-C(O)-C(O)-OR<sub>10</sub>;

10 each R<sub>9</sub> is independently selected from the group  
consisting of -Ar<sub>3</sub> and a -C<sub>1-6</sub> straight or branched  
alkyl group optionally substituted with -Ar<sub>3</sub>, wherein  
the -C<sub>1-6</sub> alkyl group is optionally unsaturated;

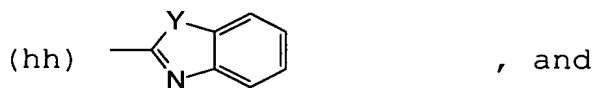
15 each R<sub>10</sub> is independently selected from the group  
consisting of -H, -Ar<sub>3</sub>, a -C<sub>3-6</sub> cycloalkyl group, and a  
-C<sub>1-6</sub> straight or branched alkyl group optionally  
substituted with -Ar<sub>3</sub>, wherein the -C<sub>1-6</sub> alkyl group is  
optionally unsaturated;

each R<sub>11</sub> is independently selected from the group  
consisting of:  
20 -Ar<sub>4</sub>,  
-(CH<sub>2</sub>)<sub>1-3</sub>-Ar<sub>4</sub>,  
-H, and  
-C(O)-Ar<sub>4</sub>;

25 R<sub>15</sub> is selected from the group consisting of -OH,  
-OAr<sub>3</sub>, -N(H)-OH, and -OC<sub>1-6</sub>, wherein C<sub>1-6</sub> is a straight  
or branched alkyl group optionally substituted with  
-Ar<sub>3</sub>, -CONH<sub>2</sub>, -OR<sub>5</sub>, -OH, -OR<sub>9</sub>, or -CO<sub>2</sub>H;

Ar<sub>2</sub> is independently selected from the following  
group, in which any ring may optionally be singly or

multiply substituted by  $-Q_1$  or phenyl, optionally substituted by  $Q_1$ :



5

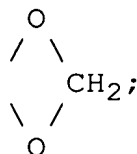
wherein each Y is independently selected from the group consisting of O and S;

each  $Ar_3$  is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings and an aromatic heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from  $-O-$ ,  $-S-$ ,  $-SO-$ ,  $SO_2$ ,  $=N-$ , and  $-NH-$ ,  $-N(R_5)-$ , and  $-N(R_9)-$  said heterocycle group optionally containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by  $-Q_1$ ;

each  $Ar_4$  is a cyclic group independently selected from the set consisting of an aryl group which contains 6, 10, 12, or 14 carbon atoms and between 1 and 3 rings, and a heterocycle group containing between 5 and 15 ring atoms and between 1 and 3 rings, said heterocyclic group containing at least one heteroatom group selected from  $-O-$ ,  $-S-$ ,  $-SO-$ ,  $SO_2$ ,  $=N-$ ,  $-NH-$ ,  $-N(R_5)-$ , and  $-N(R_9)-$  said heterocycle group optionally

containing one or more double bonds, said heterocycle group optionally comprising one or more aromatic rings, and said cyclic group optionally being singly or multiply substituted by -Q<sub>1</sub>;

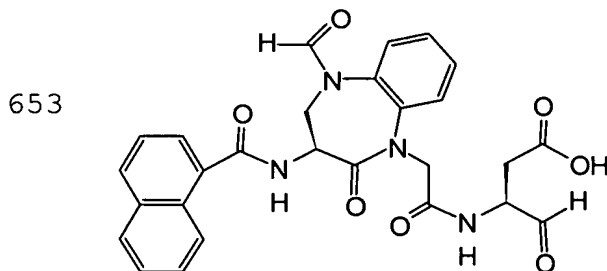
each Q<sub>1</sub> is independently selected from the group consisting of -NH<sub>2</sub>, -CO<sub>2</sub>H, -Cl, -F, -Br, -I, -NO<sub>2</sub>, -CN, =O, -OH, -perfluoro C<sub>1-3</sub> alkyl, R<sub>5</sub>, -OR<sub>5</sub>, -NHR<sub>5</sub>, -OR<sub>9</sub>, -N(R<sub>9</sub>)(R<sub>10</sub>), -R<sub>9</sub>, -C(O)-R<sub>10</sub>, and



provided that when -Ar<sub>3</sub> is substituted with a Q<sub>1</sub> group which comprises one or more additional -Ar<sub>3</sub> groups, said additional -Ar<sub>3</sub> groups are not substituted with another -Ar<sub>3</sub>.

105-111. (canceled)

112. (previously presented) The compound according to claim 104, selected from the group consisting of:





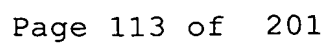
1



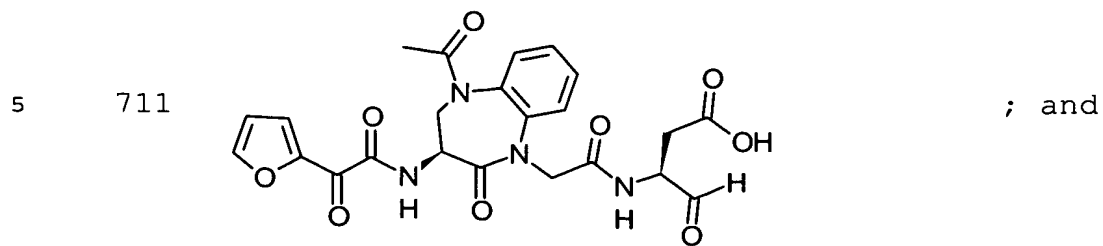
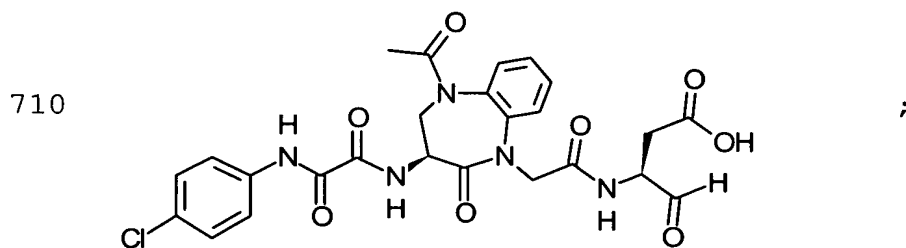
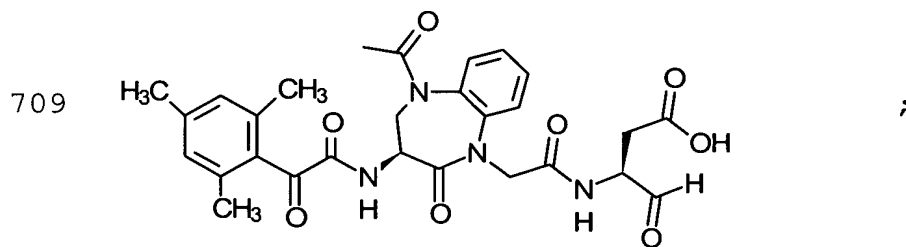
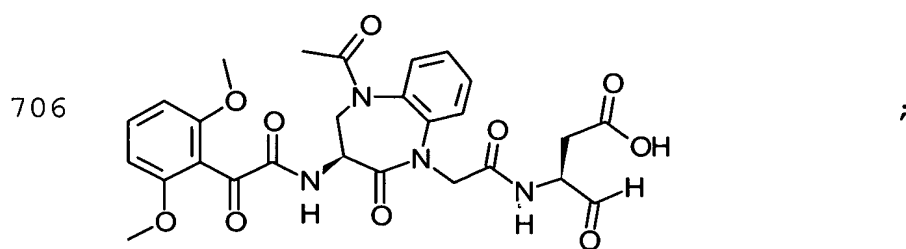
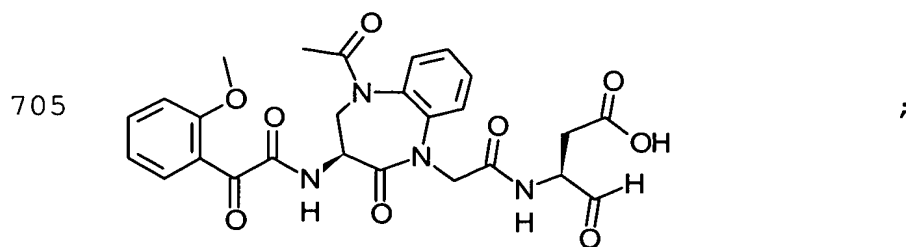
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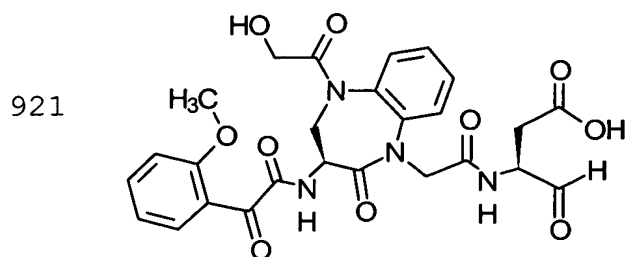


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113. (canceled)

114. (previously presented) The compound  
according to claim 68, wherein:

5 m is 1;

T<sub>1</sub> is O or S;

R<sub>21</sub> is -H or -CH<sub>3</sub>;

Ar<sub>2</sub> is (hh);

10 Y is O;

each Ar<sub>3</sub> cyclic group is independently selected  
from the set consisting of phenyl, naphthyl, thienyl,  
quinolinyl, isoquinolinyl, pyrazolyl, thiazolyl,  
15 isoxazolyl, benzotriazolyl, benzimidazolyl,  
thienothienyl, imidazolyl, thiadiazolyl,  
benzo[b]thiophenyl, pyridyl, benzofuranyl, and indolyl  
and said cyclic group being singly or multiply  
substituted by -Q<sub>1</sub>;

20 each Ar<sub>4</sub> cyclic group is independently selected  
from the set consisting of phenyl, tetrazolyl,  
pyridinyl, oxazolyl, naphthyl, pyrimidinyl, and thienyl

and said cyclic group being singly or multiply  
substituted by  
-Q<sub>1</sub>;

each Q<sub>1</sub> is independently selected from the group  
5 consisting of -NH<sub>2</sub>, -Cl, -F, -Br, -OH, -R<sub>9</sub>, -NH-R<sub>5</sub>  
wherein R<sub>5</sub> is -C(O)-R<sub>10</sub> or -S(O)<sub>2</sub>-R<sub>9</sub>, -OR<sub>5</sub> wherein R<sub>5</sub> is  
-C(O)-R<sub>10</sub>, -OR<sub>9</sub>, -NHR<sub>9</sub>, and



wherein each R<sub>9</sub> and R<sub>10</sub> are independently a -C<sub>1-6</sub>  
straight or branched alkyl group optionally substituted  
15 with -Ar<sub>3</sub> wherein Ar<sub>3</sub> is phenyl;

provided that when -Ar<sub>3</sub> is substituted with a Q<sub>1</sub>  
group which comprises one or more additional -Ar<sub>3</sub>  
groups, said additional -Ar<sub>3</sub> groups are not substituted  
20 with another -Ar<sub>3</sub>.

115-117. (canceled)

118. (previously presented) The compound  
according to claims 104 or 114, wherein R<sub>5</sub> is -C(O)-R<sub>10</sub>  
or -C(O)C(O)-R<sub>10</sub>.

25 119. (previously presented) The compound  
according to claim 118, wherein R<sub>10</sub> is Ar<sub>3</sub>.

120. (previously presented) The compound  
according to claim 119, wherein:

R<sub>5</sub> is -C(O)-R<sub>10</sub> and R<sub>10</sub> is Ar<sub>3</sub>, wherein the Ar<sub>3</sub>

cyclic group is phenyl optionally being singly or multiply substituted by:

-R<sub>9</sub>, wherein R<sub>9</sub> is a C<sub>1-4</sub> straight or branched alkyl group;

5        -F,

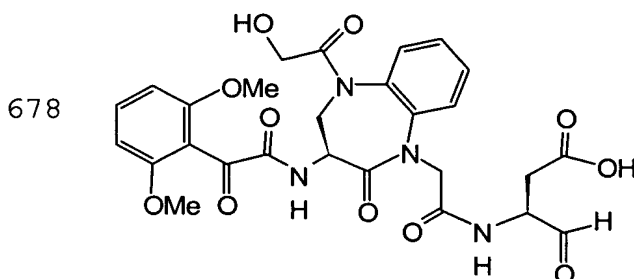
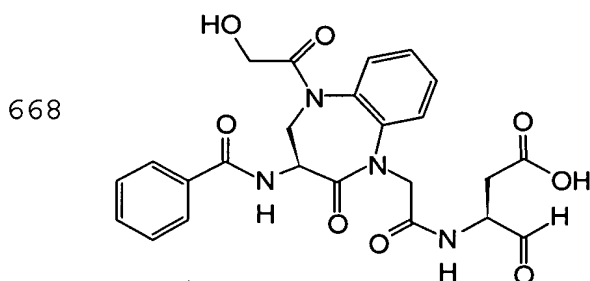
         -Cl,

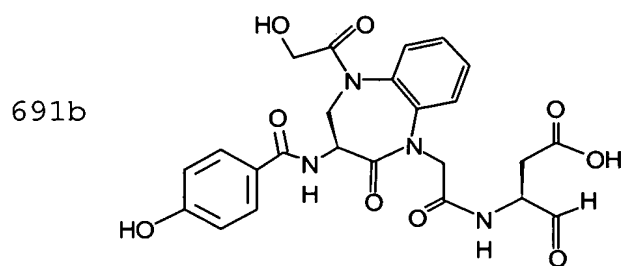
         -N(H)-R<sub>5</sub>, wherein -R<sub>5</sub> is -H or -C(O)-R<sub>10</sub>, wherein R<sub>10</sub> is a -C<sub>1-6</sub> straight or branched alkyl group optionally substituted with -Ar<sub>3</sub>, wherein Ar<sub>3</sub> is  
10        phenyl,

         -N(R<sub>9</sub>)(R<sub>10</sub>), wherein R<sub>9</sub> and R<sub>10</sub> are independently a -C<sub>1-4</sub> straight or branched alkyl group, or

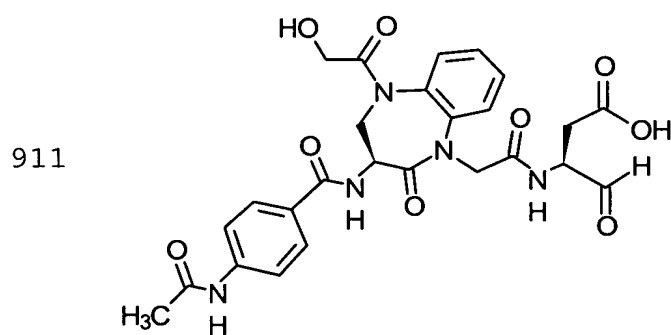
         -O-R<sub>5</sub>, wherein R<sub>5</sub> is H or a -C<sub>1-4</sub> straight or branched alkyl group.

15                    121. (previously presented) The compound according to claim 120, selected from the group consisting of:

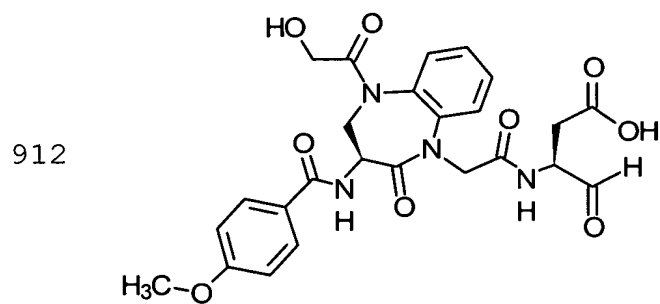




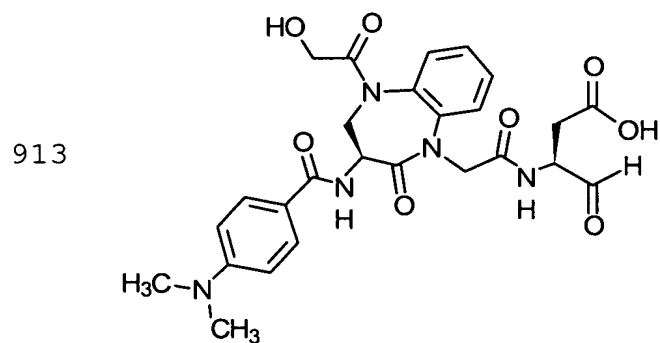
;



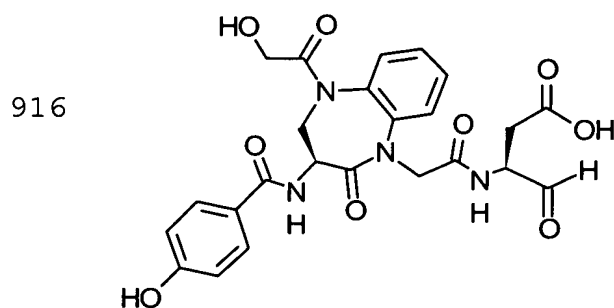
;



;

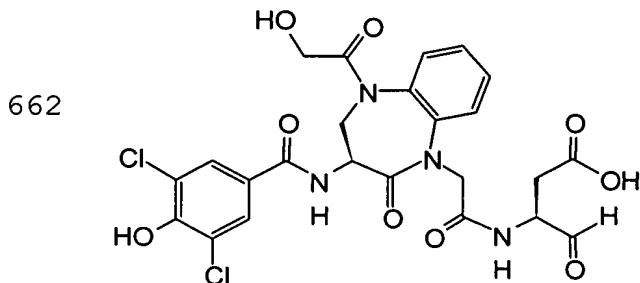
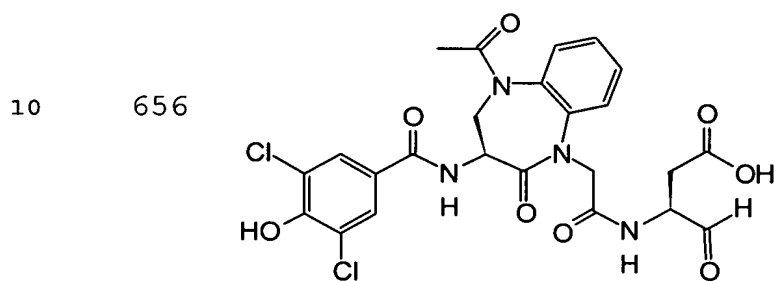


; and

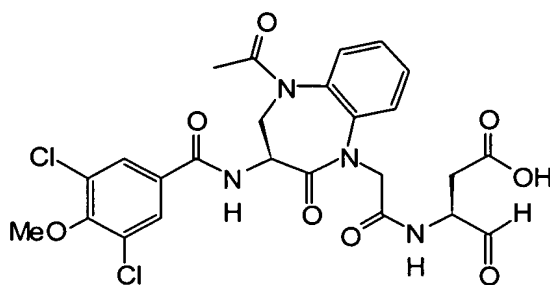


122. (previously presented) The compound according to claim 120, wherein Ar<sub>3</sub> is phenyl being singly or multiply substituted at the 3- or 5-position by -Cl or at the 4-position by -NH-R<sub>5</sub>, -N(R<sub>9</sub>)(R<sub>10</sub>), or -O-R<sub>5</sub>.

123. (previously presented) The compound according to claim 122, selected from the group consisting of:

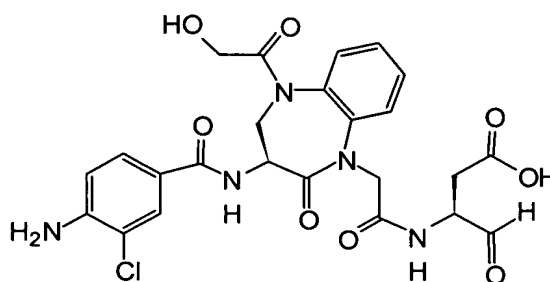


669



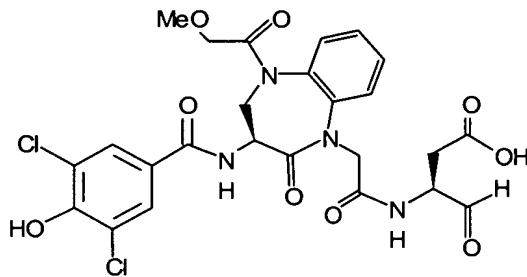
;

686



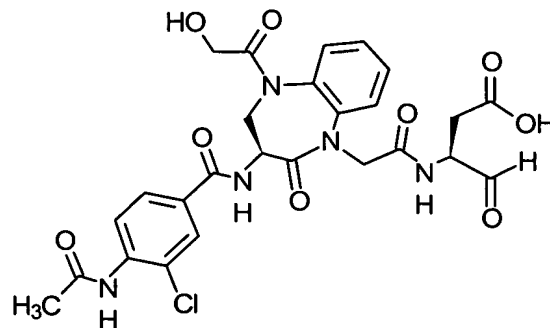
;

689a



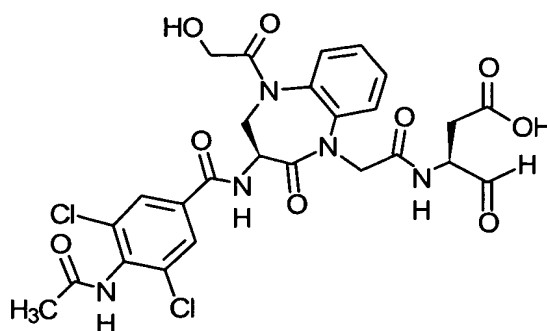
;

914



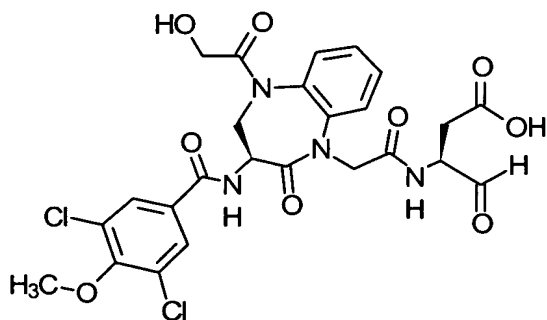
;

915



; and

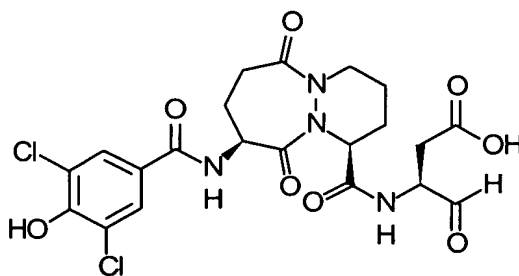
918



.

124. (previously presented) The compound  
according to claim 122, selected from the group  
5 consisting of:

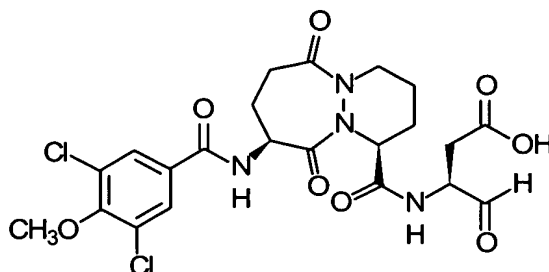
214k



; and



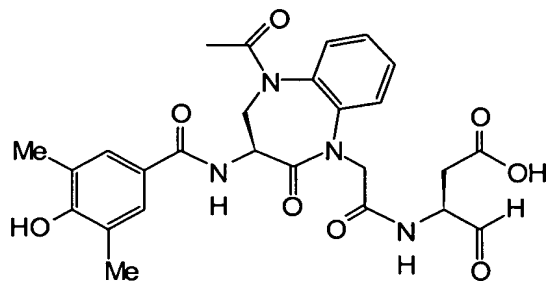
214m



125. (previously presented) The compound according to claim 120, wherein  $\text{Ar}_3$  is phenyl being singly or multiply substituted at the 3- or 5-position by  $-\text{R}_9$ , wherein  $\text{R}_9$  is a  $\text{C}_{1-4}$  straight or branched alkyl group;  
5 and at the 4-position by  $-\text{O}-\text{R}_5$ .

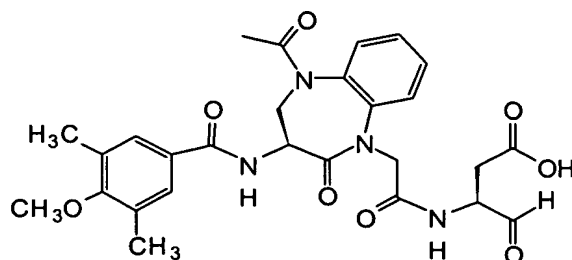
126. (previously presented) The compound according to claim 125, selected from the group  
10 consisting of:

671

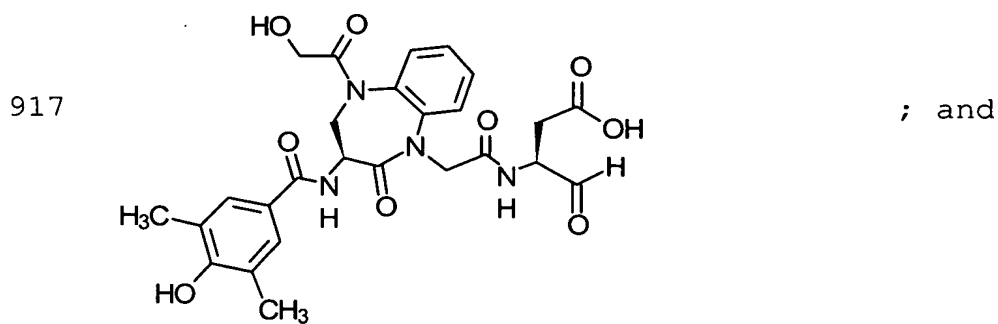
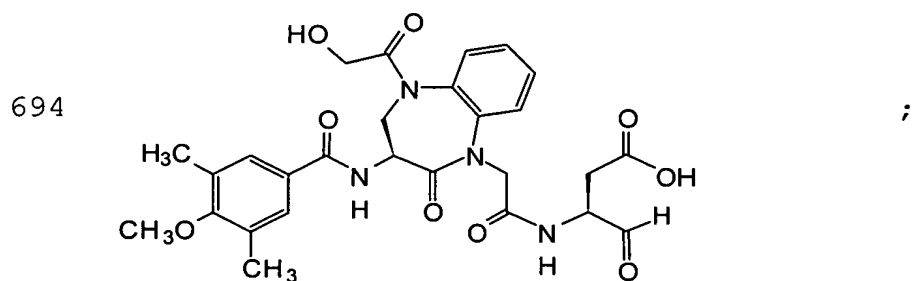
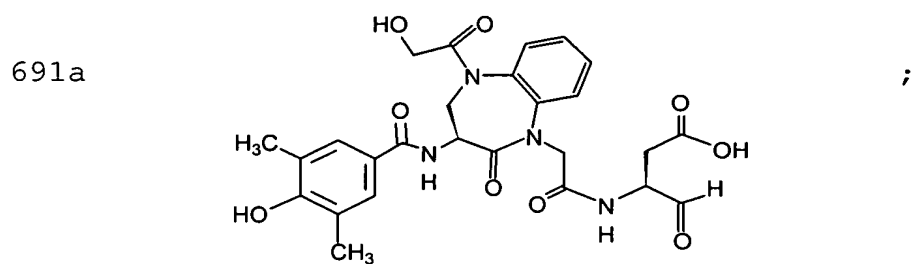
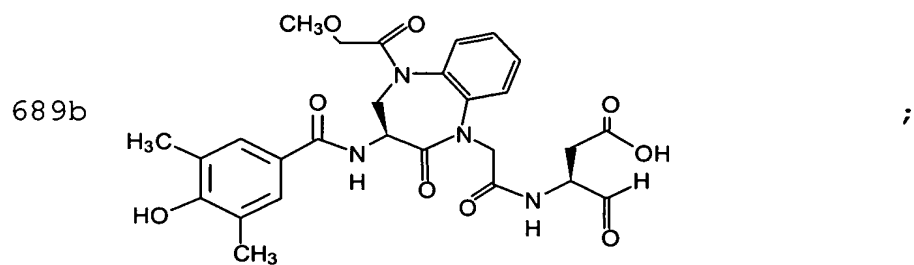


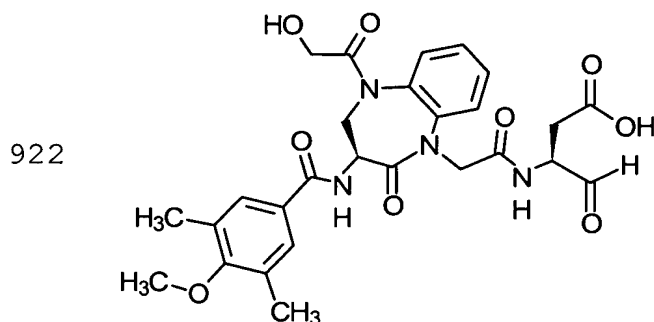
;

684



;

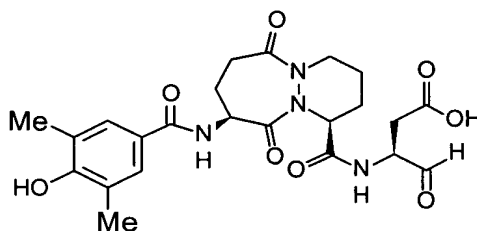




127. (previously presented) The compound according to claim 125, wherein the compound is:

214w

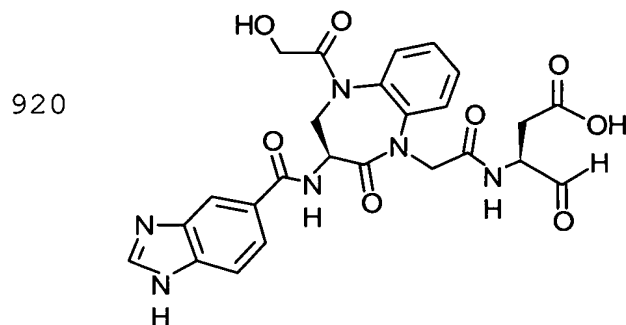
5



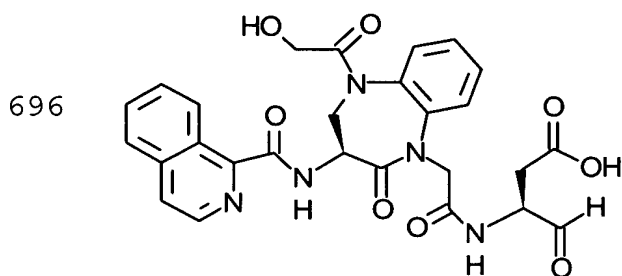
128. (previously presented) The compound according to claim 119, wherein:

10  $R_5$  is  $-C(O)-R_{10}$ , wherein  $R_{10}$  is  $Ar_3$  and the  $Ar_3$  cyclic group is selected from the group consisting of is indolyl, benzimidazolyl, thienyl, quinolyl, isoquinolyl and benzo[b]thiophenyl, and said cyclic group optionally being singly or multiply substituted by  $-Q_1$ .

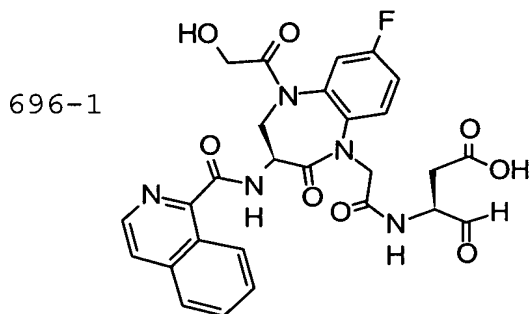
15 129. (previously presented) The compound according to claim 128, selected from the group consisting of:



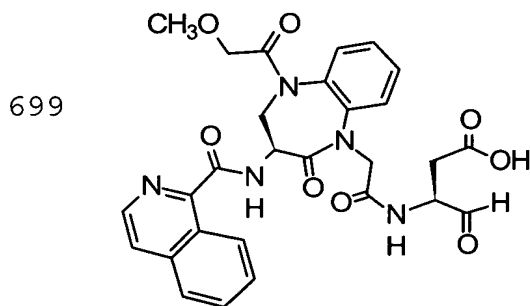
131. (previously presented) The compound according to claim 130, wherein the compound is:



;



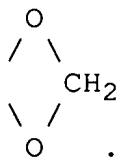
; and



132. (canceled)

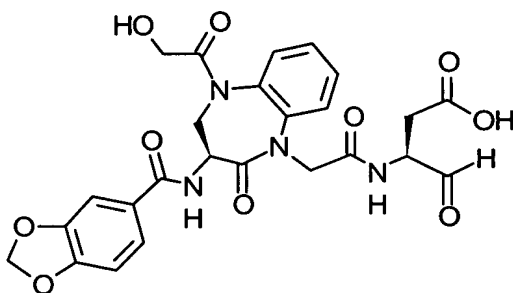
5                    133. (previously presented) The compound according to claim 119, wherein  $R_5$  is  $-C(O)-R_{10}$ , wherein  $R_{10}$  is  $Ar_3$  and the  $Ar_3$  cyclic group is phenyl, substituted by

5



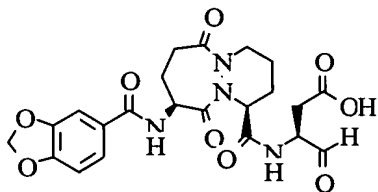
134. (previously presented) The compound according to claim 133, wherein the compound is:

910



10 135. (previously presented) The compound according to claim 133, wherein the compound is:

415



136-137. (canceled)

15 138. (previously presented) A method for treating or preventing a disease selected from an IGIF mediated disease, an IFN- $\gamma$  mediated disease, an inflammatory disease, an autoimmune disease, an infectious disease, a proliferative disease, a neurodegenerative disease, a necrotic disease,

osteoarthritis, acute pancreatitis, chronic  
pancreatitis, asthma, rheumatoid arthritis,  
inflammatory bowel disease, Crohn's disease, ulcerative  
collitis, cerebral ischemia, myocardial ischemia, adult  
5 respiratory distress syndrome, infectious hepatitis,  
sepsis, septic shock, Shigellosis, glomerulonephritis,  
systemic lupus erythematosus, scleroderma, chronic  
thyroiditis, Graves' disease, autoimmune gastritis,  
insulin-dependent diabetes mellitus (Type I), juvenile  
10 diabetes, autoimmune hemolytic anemia, autoimmune  
neutropenia, thrombocytopenia, myasthenia gravis,  
multiple sclerosis, psoriasis, lichenplanus, graft vs.  
host disease, acute dermatomyositis, eczema, primary  
cirrhosis, hepatitis, uveitis, Behcet's disease, acute  
15 dermatomyositis, atopic skin disease, pure red cell  
aplasia, aplastic anemia, amyotrophic lateral sclerosis  
and nephrotic syndrome comprising the step of  
administering to said patient a pharmaceutical  
composition according to claim 42.

20 139. (previously presented) The method  
according to claim 138, wherein the disease is selected  
from an inflammatory disease, an autoimmune disease, an  
infectious disease, rheumatoid arthritis, ulcerative  
collitis, Crohn's disease, hepatitis, adult respiratory  
25 distress syndrome, glomerulonephritis,  
insulin-dependent diabetes mellitus (Type I), juvenile  
diabetes, psoriasis, graft vs. host disease, and  
hepatitis.

140-153. (canceled)

154. (previously presented) A method for preventing or treating inflammation, comprising contacting a cell population with an inhibiting effective amount of a reagent that suppresses the protease activity of at least one member of the interleukin-1beta-converting enzyme (ICE)/CED-3 family, thereby preventing or treating inflammation, wherein said inflammation is due to an inflammatory disease, and wherein said inflammatory disease is selected from the group consisting of arthritis, cholangitis, colitis, encephalitis, endocervicitis, hepatitis, pancreatitis, and reperfusion injury.

155. (currently amended) The method of claim 154 ~~135~~, wherein said inflammation is chronic inflammation.

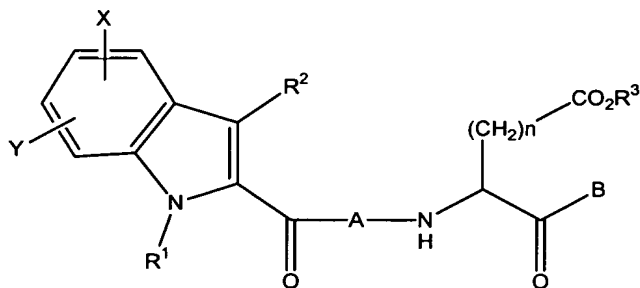
156. (currently amended) The method of claim 154 ~~135~~, wherein said inflammation is acute inflammation.

157. (currently amended) The method of claim 154 ~~135~~, wherein the reagent suppresses the protease activity in an irreversible manner.

158. (currently amended) The method of claim 154 ~~135~~, wherein the reagent suppresses the protease activity in a reversible manner.

159. (currently amended) The method of claim 154 ~~135~~, wherein the reagent is a compound of formula 1:





FORMULA 1

wherein:

n is 1 or 2;

R<sup>1</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
5 (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
or (CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup>, wherein m=1-4, and R<sup>4</sup> is as defined  
below;

R<sup>2</sup> is a hydrogen atom, chloro, alkyl, cycloalkyl,  
10 (cycloalkyl)alkyl, phenyl, (substituted)phenyl,  
phenylalkyl, (substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl or (CH<sub>2</sub>)<sub>p</sub>CO<sub>2</sub>R<sup>5</sup>, wherein p=0-4, and R<sup>5</sup>  
is as defined below;

R<sup>3</sup> is a hydrogen atom, alkyl, cycloalkyl,  
15 (cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

R<sup>4</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

20 R<sup>5</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, (substituted)phenyl, phenylalkyl, (substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl, halomethyl,  $\text{CH}_2\text{ZR}^6$ ,  $\text{CH}_2\text{OCO}(\text{aryl})$ ,  $\text{CH}_2\text{OCO}(\text{heteroaryl})$ ; or  $\text{CH}_2\text{OPO}(\text{R}_7)\text{R}_8$ ; where Z is an oxygen or a sulfur atom;

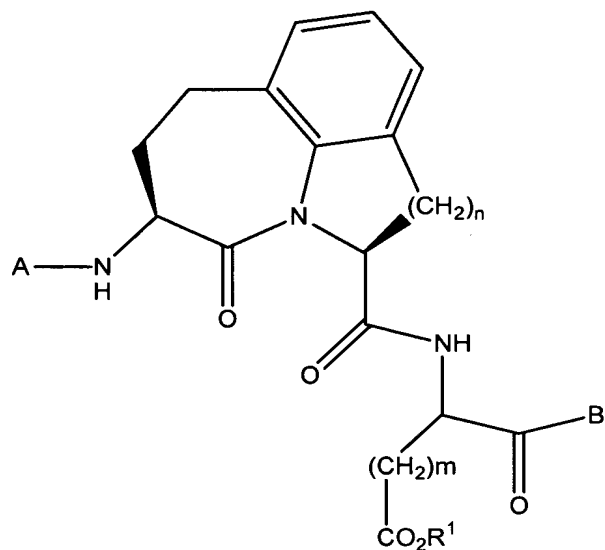
$\text{R}^6$  is phenyl, substituted phenyl, phenylalkyl, substituted phenylalkyl, heteroaryl, or (heteroaryl)alkyl; and

$\text{R}^7$  and  $\text{R}^8$  are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl, (substituted phenyl) alkyl, and (cycloalkyl) alkyl; and

X and Y are independently selected from the group consisting of a hydrogen atom, halo, trihalomethyl, amino, protected amino, an amino salt, mono-substituted amino, di-substituted amino, carboxy, protected carboxy, a carboxylate salt, hydroxy, protected hydroxy, a salt of a hydroxy group, lower alkoxy, lower alkylthio, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, (cycloalkyl)alkyl, substituted (cycloalkyl)alkyl, phenyl, substituted phenyl, phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

160. (currently amended) The method of claim ~~154~~ 154, wherein the reagent is a compound of formula 3:



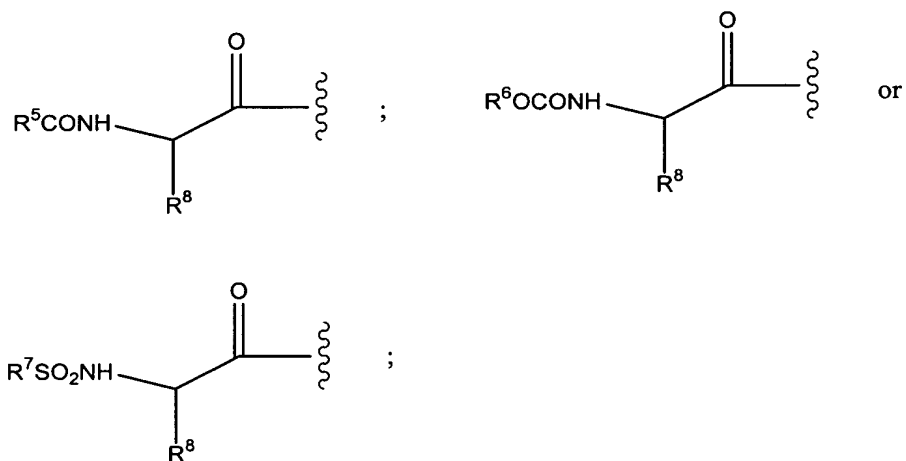
FORMULA 3

wherein:

n is 1 or 2;

5 m is 1 or 2;

A is  $R^2CO-$ ,  $R^3-O-CO-$ , or  $R^4SO_2-$ , a group of the formula:



further wherein:

R<sup>1</sup> is a hydrogen atom, alkyl or phenylalkyl;

R<sup>2</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
5 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>3</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl,  
phenylalkyl, or (substituted phenyl)alkyl;

R<sup>4</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
10 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>5</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

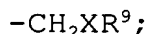
R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl,  
15 phenylalkyl, or (substituted phenyl)alkyl;

R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>8</sup> is an amino acid side chain chosen from the  
20 group consisting of natural and unnatural amino acids;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl,  
substituted phenyl, (substituted phenyl)alkyl,  
heteroaryl, (heteroaryl)alkyl, or halomethyl;

25 a group of the formula:

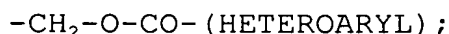


wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl,  
(substituted phenyl)alkyl, heteroaryl, or  
(heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

30 a group of the formula:



a group of the formula:



a group of the formula:

-CH<sub>2</sub>-O-PO(R<sup>10</sup>)R<sup>11</sup> wherein R<sup>10</sup> and R<sup>11</sup> are  
independently selected from a group consisting of  
alkyl, cycloalkyl, phenyl, substituted phenyl,  
5 phenylalkyl and (substituted phenyl) alkyl; and the  
pharmaceutically-acceptable salts thereof.

161. (New) A method for preventing or  
treating inflammation, comprising contacting a cell  
10 population with an inhibiting effective amount of a  
reagent that suppresses the protease activity of at  
least one member of the interleukin-1 beta-converting  
enzyme (ICE)/CED-3 family, thereby preventing or  
treating inflammation.

15 162. (New) The method of claim 161, wherein  
said inflammation is chronic inflammation.

163. (New) The method of claim 161, wherein  
said inflammation is acute inflammation.

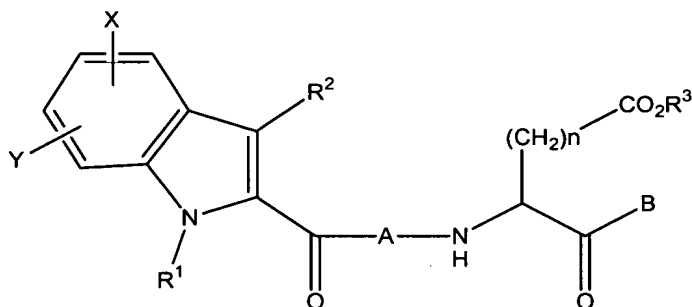
20 164. (New) The method of claim 161, wherein  
said inflammation is due to an inflammatory disease.

165. (New) The method of claim 164, wherein  
said inflammatory disease is selected from the group  
consisting of septic shock, septicemia, and adult  
respiratory distress syndrome.

25 166. (New) The method of claim 161, wherein  
the reagent suppresses the protease activity in an  
irreversible manner.

167. (New) The method of claim 161, wherein the reagent suppresses the protease activity in a reversible manner.

168. (New) The method of claim 161, wherein  
5 the reagent is a compound of formula 1:



FORMULA 1

wherein:

$n$  is 1 or 2;

$R^1$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
10 (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
or  $(CH_2)_mCO_2R^4$ , wherein  $m=1-4$ , and  $R^4$  is as defined  
below;

$R^2$  is a hydrogen atom, chloro, alkyl, cycloalkyl,  
15 (cycloalkyl)alkyl, phenyl, (substituted)phenyl,  
phenylalkyl, (substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl or  $(CH_2)_pCO_2R^5$ , wherein  $p=0-4$ , and  $R^5$   
is as defined below;

$R^3$  is a hydrogen atom, alkyl, cycloalkyl,  
20 (cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

R<sup>4</sup> is a hydrogen atom alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

5 R<sup>5</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

A is a natural and unnatural amino acid;

10 B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl, halomethyl, CH<sub>2</sub>ZR<sup>6</sup>, CH<sub>2</sub>OCO(aryl),  
CH<sub>2</sub>OCO(heteroaryl); or CH<sub>2</sub>OPO(R<sup>7</sup>)R<sup>8</sup>

where Z is an oxygen or a sulfur atom;

15 R<sup>6</sup> is phenyl, substituted phenyl, phenylalkyl,  
substituted phenylalkyl, heteroaryl, or  
(heteroaryl)alkyl; and

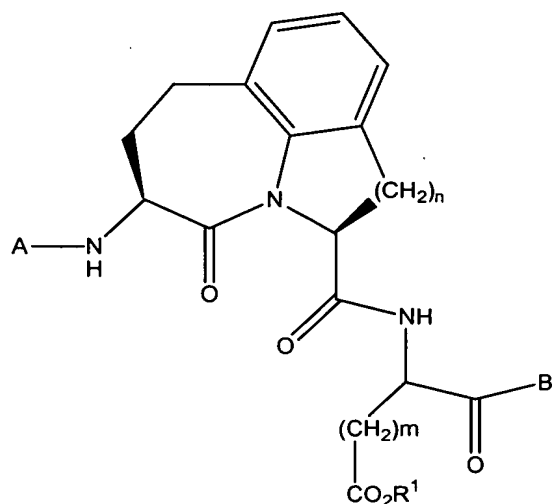
20 R<sup>7</sup> and R<sup>8</sup> are independently selected from a group  
consisting of alkyl, cycloalkyl, phenyl, substituted  
phenyl, phenylalkyl, (substituted phenyl) alkyl, and  
(cycloalkyl) alkyl; and

25 X and Y are independently selected from the group  
consisting of a hydrogen atom, halo, trihalomethyl,  
amino, protected amino, an amino salt, mono-substituted  
amino, di-substituted amino, carboxy, protected  
carboxy, a carboxylate salt, hydroxy, protected

hydroxy, a salt of a hydroxy group, lower alkoxy, lower  
alkylthio, alkyl, substituted alkyl, cycloalkyl,  
substituted cycloalkyl, (cycloalkyl)alkyl, substituted  
(cycloalkyl)alkyl, phenyl, substituted phenyl,  
5 phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

169. (New) The method of claim 161, wherein  
the reagent is a compound of formula 3:



FORMULA 3  
wherein:

10

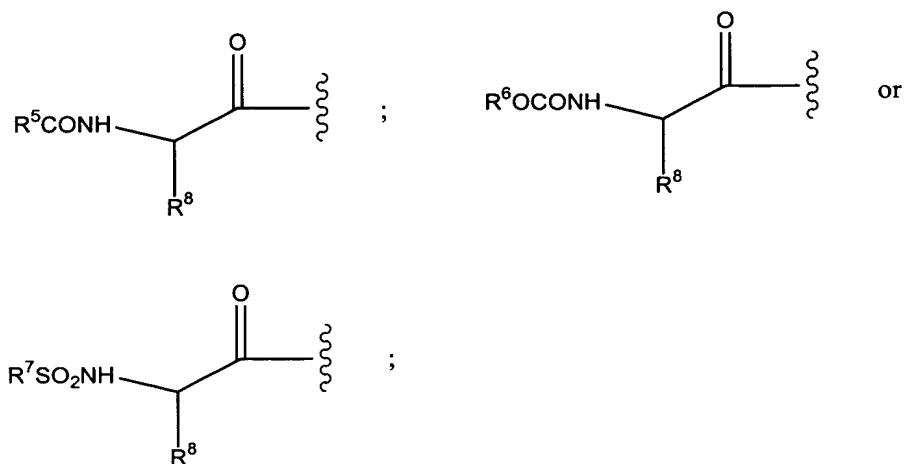
n is 1 or 2;

m is 1 or 2;

A is R<sup>2</sup>CO-, R<sup>3</sup>-O-CO-, or R<sup>4</sup>SO<sub>2</sub>-;

a group of the formula:





further wherein:

R<sup>1</sup> is a hydrogen atom, alkyl or phenylalkyl;

R<sup>2</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
 phenylalkyl, substituted phenyl, (substituted  
 5 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>3</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl,  
 or (substituted phenyl)alkyl;

R<sup>4</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
 phenylalkyl, substituted phenyl, (substituted  
 10 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>5</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
 phenylalkyl, substituted phenyl, (substituted  
 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

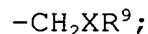
R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl,  
 15 or (substituted phenyl)alkyl;

R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

5 R<sup>8</sup> is an amino acid side chain chosen from the group consisting of natural and unnatural amino acids;

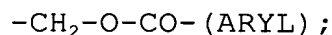
B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, (heteroaryl)alkyl, or halomethyl;

10 a group of the formula:

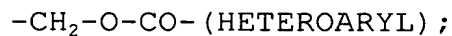


wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

15 a group of the formula:



a group of the formula:



a group of the formula:

20  $-\text{CH}_2-\text{O}-\text{PO}(\text{R}^{10})\text{R}^{11}$

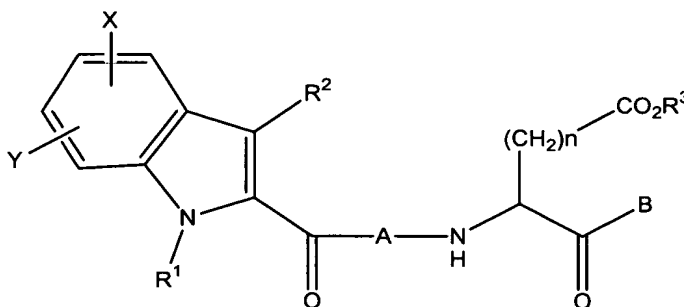
wherein  $R^{10}$  and  $R^{11}$  are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl and (substituted phenyl) alkyl; and the pharmaceutically-acceptable salts thereof.

170. (New) A composition comprising a cosmetic, a reagent that suppresses the protease activity of at least one member of the interleukin-1 beta-converting enzyme (ICE)/CED-3 family and a cosmetically or dermatologically acceptable carrier, adapted for preventing or ameliorating irritation of the skin of a mammal due to said cosmetic.

171. (New) The composition of claim 170, wherein the reagent suppresses the protease activity in an irreversible manner.

172. (New) The composition of claim 170, wherein the reagent suppresses the protease activity in a reversible manner.

173. (New) The composition of claim 170, wherein the reagent is a compound of formula 1:



FORMULA 1

wherein:

n is 1 or 2;

R<sup>1</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
5 (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
or (CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup> wherein m=1-4, and R<sup>4</sup> is as defined below;

R<sup>2</sup> is a hydrogen atom, chloro, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenyl, (substituted)phenyl,  
10 phenylalkyl, (substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl or (CH<sub>2</sub>)<sub>p</sub>CO<sub>2</sub>R<sup>5</sup>, wherein p=0-4, and R<sup>5</sup>  
is as defined below;

R<sup>3</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
15 (substituted)phenylalkyl;

R<sup>4</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

R<sup>5</sup> is a hydrogen atom, alkyl, cycloalkyl,  
20 (cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl,  
25 (substituted)phenyl, phenylalkyl,

(substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl, halomethyl,  $\text{CH}_2\text{ZR}^6$ ,  $\text{CH}_2\text{OCO}(\text{aryl})$ ,  
 $\text{CH}_2\text{OCO}(\text{heteroaryl})$ ; or  $\text{CH}_2\text{OPO}(\text{R}^7)\text{R}^8$

where Z is an oxygen or a sulfur atom;

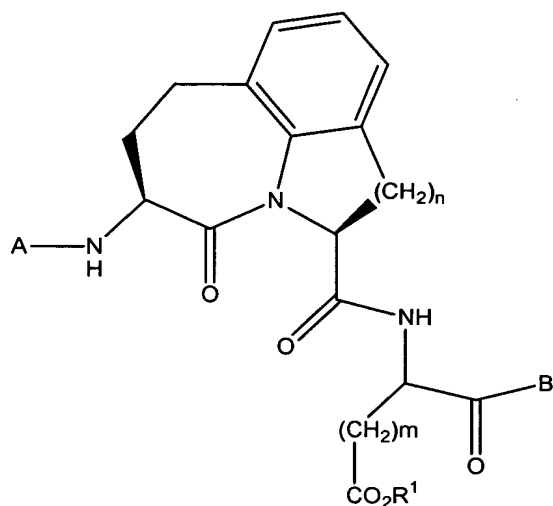
- 5      $\text{R}^6$  is phenyl, substituted phenyl, phenylalkyl,  
substituted phenylalkyl, heteroaryl, or  
(heteroaryl)alkyl; and

- $\text{R}^7$  and  $\text{R}^8$  are independently selected from a group  
consisting of alkyl, cycloalkyl, phenyl, substituted  
10     phenyl, phenylalkyl, (substituted phenyl) alkyl, and  
(cycloalkyl) alkyl; and

- X and Y are independently selected from the group  
consisting of a hydrogen atom, halo, trihalomethyl,  
amino, protected amino, an amino salt, mono-substituted  
15     amino, di-substituted amino, carboxy, protected  
carboxy, a carboxylate salt, hydroxy, protected  
hydroxy, a salt of a hydroxy group, lower alkoxy, lower  
alkylthio, alkyl, substituted alkyl, cycloalkyl,  
substituted cycloalkyl, (cycloalkyl)alkyl, substituted  
20     (cycloalkyl)alkyl, phenyl, substituted phenyl,  
phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

174. (New) The composition of claim 170,  
wherein the reagent is a compound of formula 3:



FORMULA 3

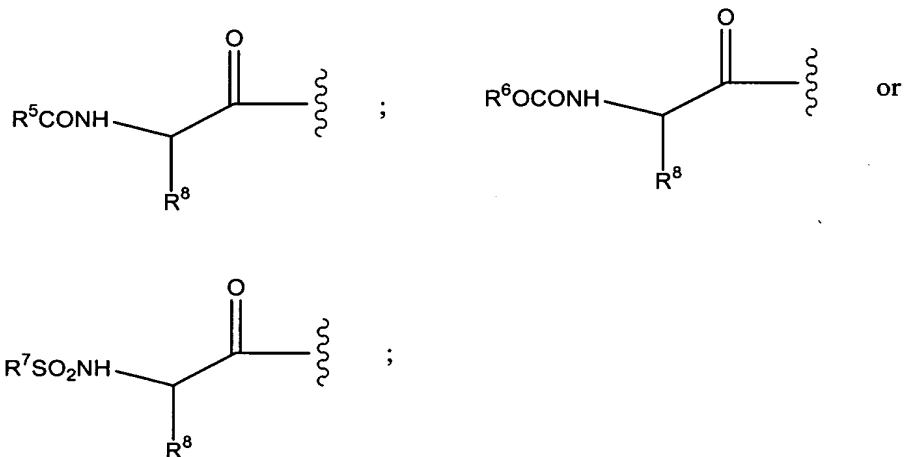
wherein:

n is 1 or 2;

m is 1 or 2;

5 A is  $R^2CO-$ ,  $R^3-O-CO-$ , or  $R^4SO_2-$ ;

a group of the formula:



further wherein:

$R^1$  is a hydrogen atom, alkyl or phenylalkyl;

R<sup>2</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

5 R<sup>3</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

R<sup>4</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

10 R<sup>5</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

15 R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>8</sup> is an amino acid side chain chosen from the group consisting of natural and unnatural amino acids;

20 B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, (heteroaryl)alkyl, or halomethyl; a group of the formula:  
--CH<sub>2</sub>XR<sup>9</sup>;

wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

a group of the formula:

5 -CH<sub>2</sub>-O-CO-(ARYL);

a group of the formula:

-CH<sub>2</sub>-O-CO-(HETEROARYL);

a group of the formula:

-CH<sub>2</sub>-O-PO(R<sup>10</sup>)R<sup>11</sup>

10 wherein R<sup>10</sup> and R<sup>11</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl and (substituted phenyl) alkyl; and the pharmaceutically-acceptable salts thereof.

15 175. (New) A method for preventing or ameliorating inflammation due to contact of the skin of a mammal with an irritant comprising contacting the skin with a reagent that suppresses the protease activity of at least one member of the  
20 interleukin-1beta-converting enzyme (ICE)/CED-3 family.

176. (New) The method of claim 175, wherein the irritant is a chemical irritant.

177. (New) The method of claim 176, wherein the chemical irritant is a cosmetic.

25 178. (New) The method of claim 176, wherein the chemical irritant is from a plant.



179. (New) The method of claim 178, wherein the plant is selected from the group consisting of Poison Ivy, Poison Oak, and Poison Sumac.

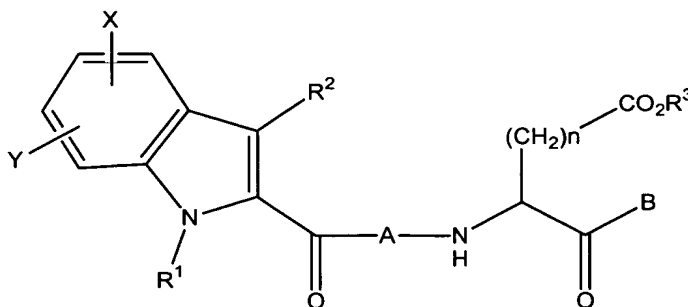
180. (New) The method of claim 175, wherein  
5 the irritant is radiation.

181. (New) The method of claim 180, wherein the radiation is ultraviolet radiation.

182. (New) The method of claim 175, wherein the reagent suppresses the protease activity in an  
10 irreversible manner.

183. (New) The method of claim 175, wherein the reagent suppresses the protease activity in a reversible manner.

184. (New) The method of claim 175, wherein  
15 the reagent is a compound of formula 1:



FORMULA 1

wherein:

n is 1 or 2;

R<sup>1</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
5 or (CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup>, wherein m=1-4, and R<sup>4</sup> is as defined  
below;

R<sup>2</sup> is a hydrogen atom, chloro, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenyl, (substituted)phenyl,  
phenylalkyl, (substituted)phenylalkyl, heteroaryl,  
10 (heteroaryl)alkyl or (CH<sub>2</sub>)<sub>p</sub>CO<sub>2</sub>R<sup>5</sup>, wherein p=0-4, and R<sup>5</sup>  
is as defined below;

R<sup>3</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

15 R<sup>4</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

R<sup>5</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
20 (substituted)phenylalkyl;

A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
25 (substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl, halomethyl, CH<sub>2</sub>ZR<sup>6</sup>, CH<sub>2</sub>OCO(aryl),  
CH<sub>2</sub>OCO(heteroaryl); or CH<sub>2</sub>OPO(R<sup>7</sup>)R<sup>8</sup>

where Z is an oxygen or a sulfur atom;

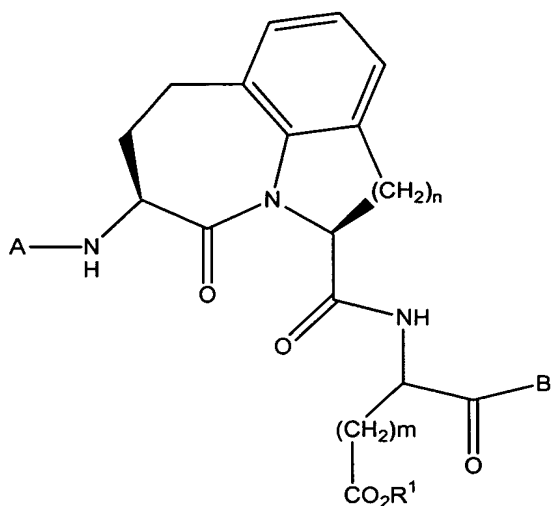
R<sup>6</sup> is phenyl, substituted phenyl, phenylalkyl, substituted phenylalkyl, heteroaryl, or (heteroaryl)alkyl; and

5 R<sup>7</sup> and R<sup>8</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl, (substituted phenyl) alkyl, and (cycloalkyl) alkyl; and

10 X and Y are independently selected from the group consisting of a hydrogen atom, halo, trihalomethyl, amino, protected amino, an amino salt, mono-substituted amino, di-substituted amino, carboxy, protected carboxy, a carboxylate salt, hydroxy, protected hydroxy, a salt of a hydroxy group, lower alkoxy, lower  
15 alkylthio, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, (cycloalkyl)alkyl, substituted (cycloalkyl)alkyl, phenyl, substituted phenyl, phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

20 185. (New) The method of claim 175, wherein the reagent is a compound of formula 3:



FORMULA 3

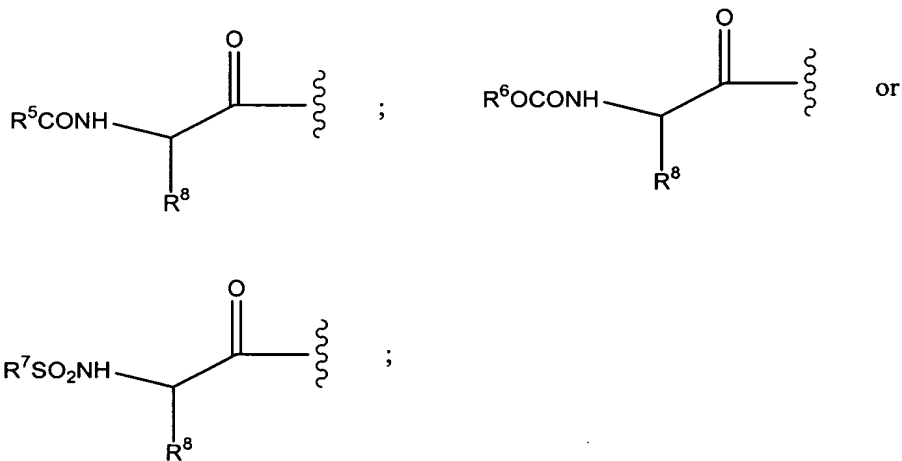
wherein:

n is 1 or 2;

m is 1 or 2;

5 A is  $R^2CO-$ ,  $R^3-O-CO-$ , or  $R^4SO_2-$ ;

a group of the formula:



further wherein:

$R^1$  is a hydrogen atom, alkyl or phenylalkyl;

R<sup>2</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

5 R<sup>3</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

R<sup>4</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

10 R<sup>5</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

15 R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>8</sup> is an amino acid side chain chosen from the group consisting of natural and unnatural amino acids;

20 B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, (heteroaryl)alkyl, or halomethyl;

a group of the formula:

--CH<sub>2</sub>XR<sup>9</sup>;

wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

a group of the formula:

5        -CH<sub>2</sub> -O-CO-(ARYL);

a group of the formula:

-CH<sub>2</sub>-O-CO-(HETEROARYL);

a group of the formula:

-CH<sub>2</sub>-O-PO(R<sup>10</sup>)R<sup>11</sup>

10        wherein R<sup>10</sup> and R<sup>11</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl and (substituted phenyl) alkyl; and the pharmaceutically-acceptable salts thereof.

15                    186. (New) A composition comprising a reagent that suppresses the protease activity of at least one member of the interleukin-1 beta-converting enzyme (ICE)/CED-3 family formulated for topical  
administration for use in preventing or ameliorating  
20        inflammation due to skin irritation.

187. (New) The composition of claim 186, wherein said formulation is selected from a lotion, a cream, a gel, a liquid, a solid, or a semisolid.

25                    188. (New) The composition of claim 186, wherein the skin irritation is due to contact of the skin with a chemical irritant.

189. (New) The composition of claim 188,  
wherein the chemical irritant is a cosmetic or an agent  
derived from a plant.

5 190. (New) The composition of claim 186,  
wherein the irritant is radiation.

191. (New) The composition of claim 186,  
wherein the irritation is due to an insect sting.

192. (New) The composition of claim 186,  
wherein the irritation is due to an insect bite.

10 193. (New) The composition of claim 186,  
wherein the irritation is due to tissue damage.

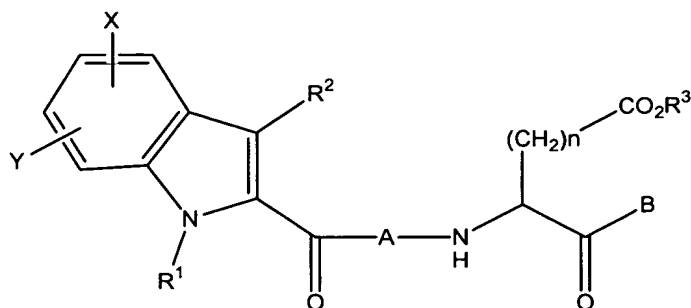
194. (New) The composition of claim 186,  
wherein the tissue damage is due to physical trauma or  
disease.

15 195. (New) The composition of claim 193,  
wherein the tissue (physical trauma or disease) damage  
is selected from the group consisting of a bum, a  
scrape, a cut, frostbite, and chemical injury.

20 196. (New) The composition of claim 186,  
wherein the reagent suppresses the protease activity in  
an irreversible manner.

197. (New) The composition of claim 186,  
wherein the reagent suppresses the protease activity in  
a reversible manner.

198. (New) The composition of claim 186,  
wherein the reagent is a compound of formula 1:



FORMULA 1

wherein:

5      n is 1 or 2;

R¹ is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
or (CH₂)<sub>m</sub>CO₂R⁴ wherein m=1-4, and R⁴ is as defined below;

10      R² is a hydrogen atom, chloro, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenyl, (substituted)phenyl,  
phenylalkyl, (substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl or (CH₂)<sub>p</sub>CO₂R⁵, wherein p=0-4, and R⁵  
is as defined below;

15      R³ is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;



R<sup>4</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

5 R<sup>5</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

A is a natural and unnatural amino acid;

10 B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl, halomethyl, CH<sub>2</sub>ZR<sup>6</sup>, CH<sub>2</sub>OCO(aryl),  
CH<sub>2</sub>OCO(heteroaryl); or CH<sub>2</sub>OPO(R<sup>7</sup>)R<sup>8</sup>

where Z is an oxygen or a sulfur atom;

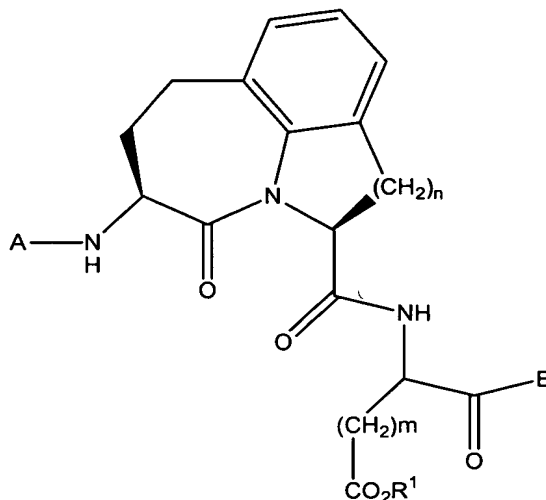
15 R<sup>6</sup> is phenyl, substituted phenyl, phenylalkyl,  
substituted phenylalkyl, heteroaryl, or  
(heteroaryl)alkyl; and

20 R<sup>7</sup> and R<sup>8</sup> are independently selected from a group  
consisting of alkyl, cycloalkyl, phenyl, substituted  
phenyl, phenylalkyl, (substituted phenyl) alkyl, and  
(cycloalkyl) alkyl; and

X and Y are independently selected from the group  
consisting of a hydrogen atom, halo, trihalomethyl,  
amino, protected amino, an amino salt, mono-substituted  
amino, di-substituted amino, carboxy, protected  
5 carboxy, a carboxylate salt, hydroxy, protected  
hydroxy, a salt of a hydroxy group, lower alkoxy, lower  
alkylthio, alkyl, substituted alkyl, cycloalkyl,  
substituted cycloalkyl, (cycloalkyl)alkyl, substituted  
(cycloalkyl)alkyl, phenyl, substituted phenyl,  
10 phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

199. (New) The composition of claim 186,  
wherein the reagent is a compound of formula 3:

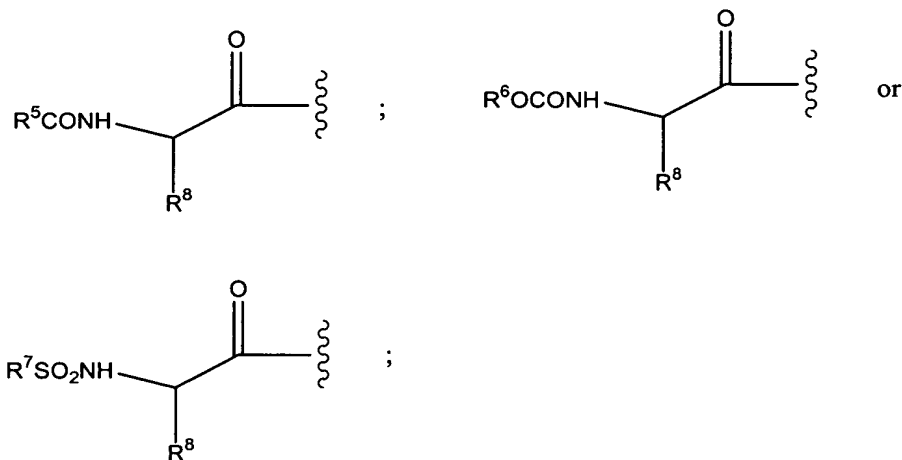


FORMULA 3

15 wherein:  
n is 1 or 2;  
m is 1 or 2;

A is  $R^2CO-$ ,  $R^3-O-CO-$ , or  $R^4SO_2-$ ;

a group of the formula:



further wherein:

$R^1$  is a hydrogen atom, alkyl or phenylalkyl;

5  $R^2$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

$R^3$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

10  $R^4$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

15  $R^5$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl,  
or (substituted phenyl)alkyl;

R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
5 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>8</sup> is an amino acid side chain chosen from the group  
consisting of natural and unnatural amino acids;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl,  
10 substituted phenyl, (substituted phenyl)alkyl,  
heteroaryl, (heteroaryl)alkyl, or halomethyl;

a group of the formula:

-CH<sub>2</sub>XR<sup>9</sup>;

wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl,  
15 (substituted phenyl)alkyl, heteroaryl, or  
(heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

a group of the formula:

-CH<sub>2</sub>-O-CO-(ARYL);

a group of the formula:

20 -CH<sub>2</sub>-O-CO-(HETEROARYL);

a group of the formula:

-CH<sub>2</sub>-O-PO(R<sup>10</sup>)R<sup>11</sup>

wherein R<sup>10</sup> and R<sup>11</sup> are independently selected from a  
group consisting of alkyl, cycloalkyl, phenyl,  
25 substituted phenyl, phenylalkyl and (substituted  
phenyl) alkyl; and the pharmaceutically-acceptable  
salts thereof.

200. (New) A method for preventing or ameliorating inflammation due to contact of a tissue of a mammal with an irritant comprising contacting said tissue with a reagent that suppresses the protease  
5 activity of at least one member of the interleukin-1 beta-converting enzyme (ICE)/CED-3 family.

201. (New) The method of claim 200, wherein the irritant is a chemical irritant.

202. (New) The method of claim 201, wherein  
10 the chemical irritant is a cosmetic.

203. (New) The method of claim 201, wherein the chemical irritant is from a plant.

204. (New) The method of claim 203, wherein the plant is selected from the group consisting of  
15 Poison Ivy, Poison Oak, and Poison Sumac.

205. (New) The method of claim 200, wherein the irritant is radiation.

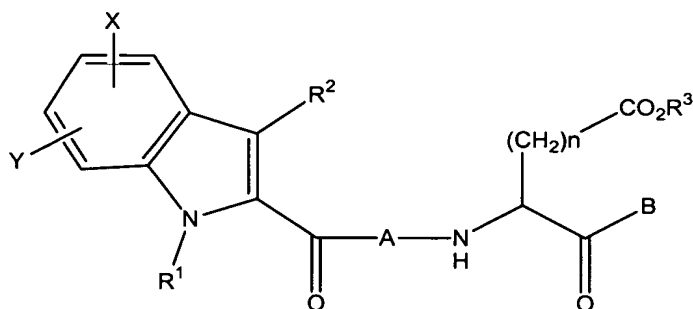
206. (New) The method of claim 205, wherein the radiation is ultraviolet radiation.

207. (New) The method of claim 200, wherein  
20 the irritant is a bacteria.

208. (New) The method of claim 200, wherein the reagent suppresses the protease activity in an irreversible manner.

209. (New) The method of claim 200, wherein the reagent suppresses the protease activity in a reversible manner.

210. (New) The method of claim 200, wherein  
5 the reagent is a compound of formula 1:



FORMULA 1

wherein:

n is 1 or 2;

R<sup>1</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
10 (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
or (CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup>, wherein m=1-4, and R<sup>4</sup> is as defined  
below;

R<sup>2</sup> is a hydrogen atom, chloro, alkyl, cycloalkyl,  
15 (cycloalkyl)alkyl, phenyl, (substituted)phenyl,  
phenylalkyl, (substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl or (CH<sub>2</sub>)<sub>p</sub>CO<sub>2</sub>R<sup>5</sup>, wherein p=0-4, and R<sup>5</sup>  
is as defined below;

R<sup>3</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

5 R<sup>4</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

R<sup>5</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

10 A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl,  
15 (heteroaryl)alkyl, halomethyl, CH<sub>2</sub>ZR<sup>6</sup>, CH<sub>2</sub>OCO(aryl),  
CH<sub>2</sub>OCO(heteroaryl); or CH<sub>2</sub>OPO(R<sup>7</sup>)R<sup>8</sup>

where Z is an oxygen or a sulfur atom;

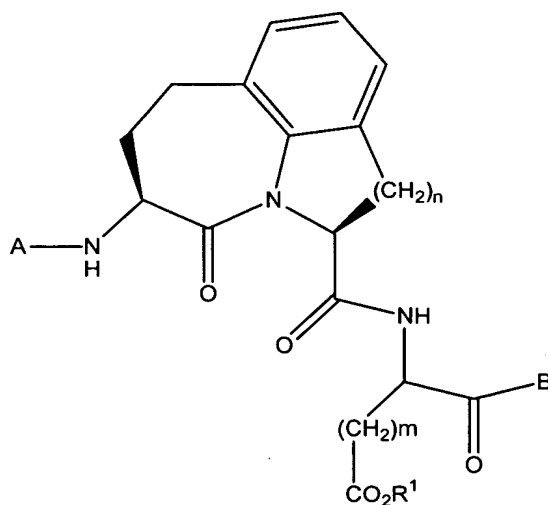
R<sup>6</sup> is phenyl, substituted phenyl, phenylalkyl,  
substituted phenylalkyl, heteroaryl, or  
20 (heteroaryl)alkyl; and

R<sup>7</sup> and R<sup>8</sup> are independently selected from a group  
consisting of alkyl, cycloalkyl, phenyl, substituted  
phenyl, phenylalkyl, (substituted phenyl) alkyl, and  
(cycloalkyl) alkyl; and

X and Y are independently selected from the group  
consisting of a hydrogen atom, halo, trihalomethyl,  
amino, protected amino, an amino salt, mono-substituted  
amino, di-substituted amino, carboxy, protected  
5 carboxy, a carboxylate salt, hydroxy, protected  
hydroxy, a salt of a hydroxy group, lower alkoxy, lower  
alkylthio, alkyl, substituted alkyl, cycloalkyl,  
substituted cycloalkyl, (cycloalkyl)alkyl, substituted  
(cycloalkyl)alkyl, phenyl, substituted phenyl,  
10 phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

211. (New) The method of claim 200, wherein  
the reagent is a compound of formula 3:



15 FORMULA 3

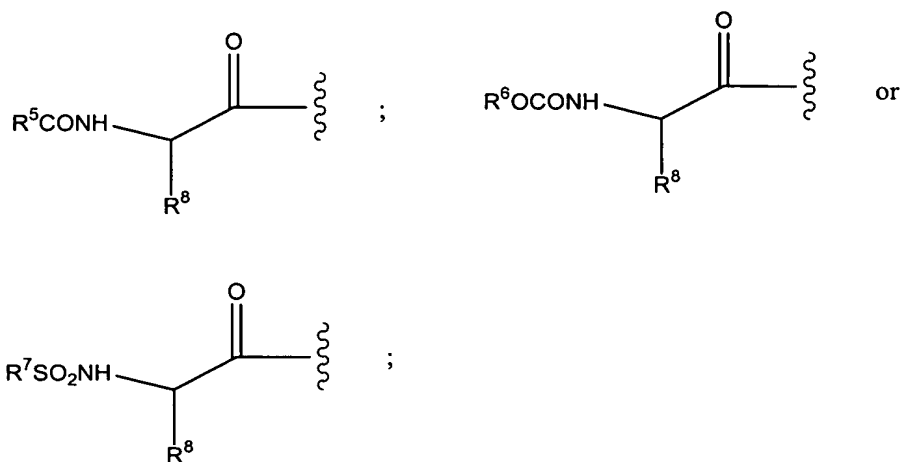
wherein:

n is 1 or 2;

m is 1 or 2;



A is  $R^2CO-$ ,  $R^3-O-CO-$ , or  $R^4SO_2-$ ;  
a group of the formula:



5 further wherein:

$R^1$  is a hydrogen atom, alkyl or phenylalkyl;

$R^2$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

10  $R^3$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

$R^4$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

15  $R^5$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

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Supp. Amdt. dated March 11, 2004

R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl,  
or (substituted phenyl)alkyl;

R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
5 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>8</sup> is an amino acid side chain chosen from the group  
consisting of natural and unnatural amino acids;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl,  
10 substituted phenyl, (substituted phenyl)alkyl,  
heteroaryl, (heteroaryl)alkyl, or halomethyl;

a group of the formula:  
-CH<sub>2</sub>XR<sup>9</sup>;

wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl,  
15 (substituted phenyl)alkyl, heteroaryl, or  
(heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

a group of the formula:  
-CH<sub>2</sub>-O-CO-(ARYL);

a group of the formula:  
20 -CH<sub>2</sub>-O-CO-(HETEROARYL);

a group of the formula:  
-CH<sub>2</sub>-O-PO(R<sup>10</sup>)R<sup>11</sup>

wherein R<sup>10</sup> and R<sup>11</sup> are independently selected from a  
group consisting of alkyl, cycloalkyl, phenyl,  
25 substituted phenyl, phenylalkyl and (substituted

phenyl) alkyl; and the pharmaceutically-acceptable salts thereof.

212. (New) A method for preventing or ameliorating inflammation associated with tissue damage comprising contacting said tissue with a reagent that suppresses the protease activity of at least one member of the interleukin-1 beta-converting enzyme (ICE)/CED-3 family.

213. (New) The method of claim 212, wherein said tissue damage is due to physical trauma.

214. (New) The method of claim 212, wherein said tissue damage is due to an autoimmune response.

215. (New) The method of claim 212, wherein said tissue damage is due to an infectious disease.

216. (New) The method of claim 212, wherein said tissue damage is due to chronic disease.

217. (New) The method of claim 212, wherein said tissue damage is spinal or brain trauma.

218. (New) The method of claim 212, wherein said tissue damage is due to an acid.

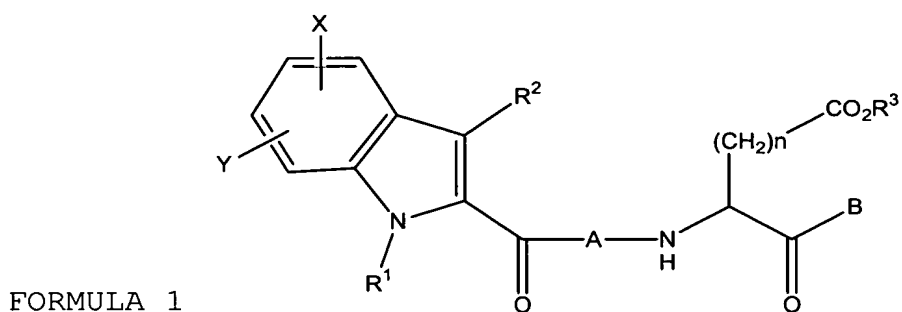
219. (New) The method of claim 212, wherein said tissue damage is due to a base.

220. (New) The method of claim 212, wherein said tissue damage is due to radiation.

221. (New) The method of claim 212, wherein the reagent suppresses the protease activity in an irreversible manner.

222. (New) The method of claim 212, wherein  
5 the reagent suppresses the protease activity in a reversible manner.

223. (New) The method of claim 212, wherein the reagent is a compound of formula 1:



10 wherein:

n is 1 or 2;

R<sup>1</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
15 or (CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup>, wherein m=1-4, and R<sup>4</sup> is as defined  
below;

R<sup>2</sup> is a hydrogen atom, chloro, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenyl, (substituted)phenyl,  
phenylalkyl, (substituted)phenylalkyl, heteroaryl,

(heteroaryl)alkyl or  $(\text{CH}_2)_p\text{CO}_2\text{R}^5$ , wherein  $p=0-4$ , and  $\text{R}^5$  is as defined below;

$\text{R}^3$  is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
5 (substituted)phenylalkyl;

$\text{R}^4$  is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

$\text{R}^5$  is a hydrogen atom, alkyl, cycloalkyl,  
10 (cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl,  
15 (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl, halomethyl,  $\text{CH}_2\text{ZR}^6$ ,  $\text{CH}_2\text{OCO}(\text{aryl})$ ,  
 $\text{CH}_2\text{OCO}(\text{heteroaryl})$ ; or  $\text{CH}_2\text{OPO}(\text{R}^7)\text{R}^8$

where Z is an oxygen or a sulfur atom;

20  $\text{R}^6$  is phenyl, substituted phenyl, phenylalkyl,  
substituted phenylalkyl, heteroaryl, or  
(heteroaryl)alkyl; and

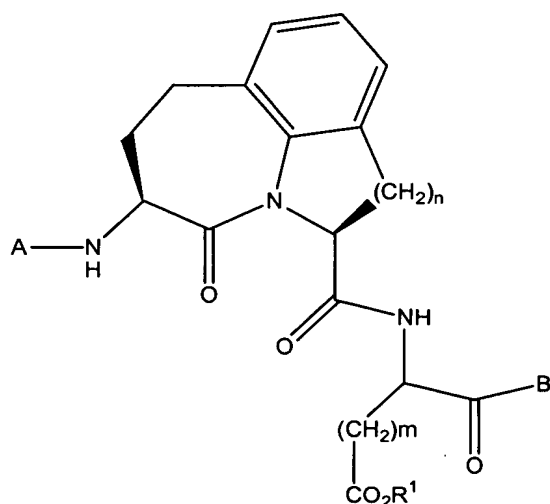
$\text{R}^7$  and  $\text{R}^8$  are independently selected from a group  
consisting of alkyl, cycloalkyl, phenyl, substituted

phenyl, phenylalkyl, (substituted phenyl) alkyl, and  
(cycloalkyl) alkyl; and

X and Y are independently selected from the group  
consisting of a hydrogen atom, halo, trihalomethyl,  
5 amino, protected amino, an amino salt, mono-substituted  
amino, di-substituted amino, carboxy, protected  
carboxy, a carboxylate salt, hydroxy, protected  
hydroxy, a salt of a hydroxy group, lower alkoxy, lower  
alkylthio, alkyl, substituted alkyl, cycloalkyl,  
10 substituted cycloalkyl, (cycloalkyl)alkyl, substituted  
(cycloalkyl)alkyl, phenyl, substituted phenyl,  
phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

15 224. (New) The method of claim 212, wherein  
the reagent is a compound of formula 3:



FORMULA 3

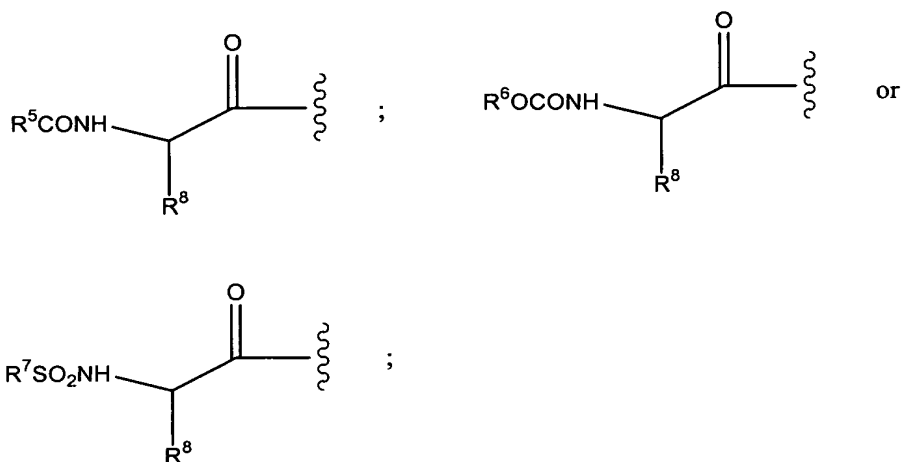
wherein:

n is 1 or 2;

m is 1 or 2;

A is  $R^2CO-$ ,  $R^3-O-CO-$ , or  $R^4SO_2-$ ;

a group of the formula:



5 further wherein:

$R^1$  is a hydrogen atom, alkyl or phenylalkyl;

$R^2$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

10  $R^3$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

$R^4$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>5</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

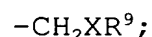
5 R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

10 R<sup>8</sup> is an amino acid side chain chosen from the group consisting of natural and unnatural amino acids;

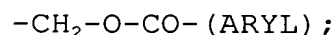
B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, (heteroaryl)alkyl, or halomethyl;

15 a group of the formula:

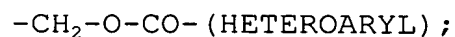


wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

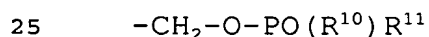
20 a group of the formula:



a group of the formula:



a group of the formula:





wherein R<sup>10</sup> and R<sup>11</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl and (substituted phenyl) alkyl; and the pharmaceutically-acceptable  
5 salts thereof.

225. (New) A composition comprising a reagent that suppresses the protease activity of at least one member of the interleukin-1beta-converting enzyme (ICE)/CED-3 family and a pharmaceutical,  
10 dermatological, or cosmetic carrier formulated for topical application to the skin or mucus membrane of an animal.

226. (New) The composition of claim 225, wherein said composition ameliorates symptoms  
15 associated with an inflammatory response.

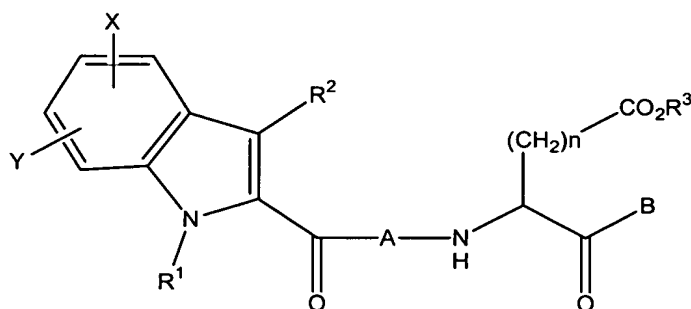
227. (New) The composition of claim 226, wherein said symptoms comprise itching, redness, or swelling.

228. (New) The composition of claim 225, wherein said composition is useful in decreasing loss  
20 of collagen or maintaining skin elasticity and appearance.

229. (New) The composition of claim 225, wherein the reagent suppresses the protease activity in  
25 an irreversible manner.

230. (New) The composition of claim 225,  
wherein the reagent suppresses the protease activity in  
a reversible manner.

231. (New) The composition of claim 225,  
5 wherein the reagent is a compound of formula 1:



FORMULA 1

wherein:

n is 1 or 2;

10  $R^1$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
or  $(CH_2)_mCO_2R^4$ , wherein  $m=1-4$ , and  $R^4$  is as defined  
below;

15  $R^2$  is a hydrogen atom, chloro, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenyl, (substituted)phenyl,  
phenylalkyl, (substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl or  $(CH_2)_pCO_2R^5$ , wherein  $p=0-4$ , and  $R^5$   
is as defined below;

R<sup>3</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

5 R<sup>4</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

R<sup>5</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

10 A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl,  
15 (heteroaryl)alkyl, halomethyl, CH<sub>2</sub>ZR<sup>6</sup>, CH<sub>2</sub>OCO(aryl),  
CH<sub>2</sub>OCO(heteroaryl); or CH<sub>2</sub>OPO(R<sup>7</sup>)R<sup>8</sup>

where Z is an oxygen or a sulfur atom;

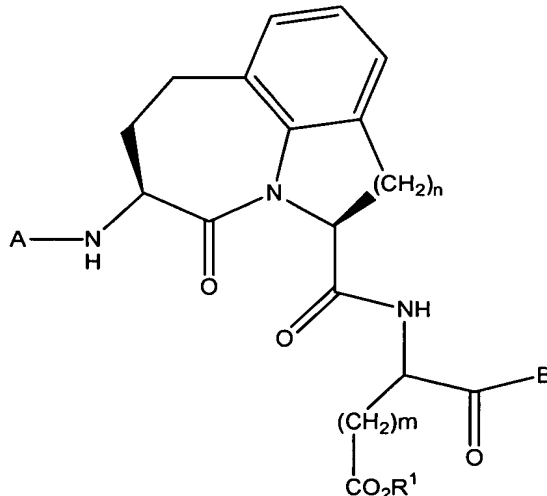
R<sup>6</sup> is phenyl, substituted phenyl, phenylalkyl,  
substituted phenylalkyl, heteroaryl, or  
20 (heteroaryl)alkyl; and

R<sup>7</sup> and R<sup>8</sup> are independently selected from a group  
consisting of alkyl, cycloalkyl, phenyl, substituted  
phenyl, phenylalkyl, (substituted phenyl) alkyl, and  
(cycloalkyl) alkyl; and

X and Y are independently selected from the group consisting of a hydrogen atom, halo, trihalomethyl, amino, protected amino, an amino salt, mono-substituted amino, di-substituted amino, carboxy, protected carboxy, a carboxylate salt, hydroxy, protected hydroxy, a salt of a hydroxy group, lower alkoxy, lower alkylthio, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, (cycloalkyl)alkyl, substituted (cycloalkyl)alkyl, phenyl, substituted phenyl, phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

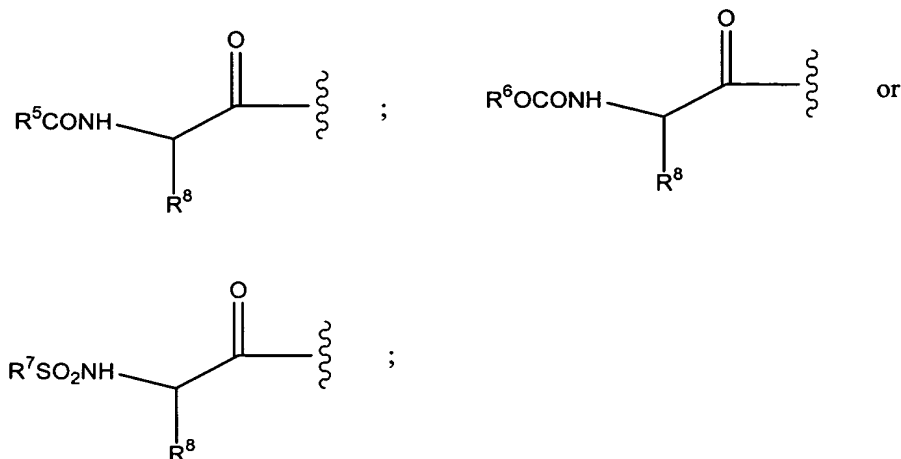
232. (New) The composition of claim 225, wherein the reagent is a compound of formula 3:



FORMULA 3

wherein:  
n is 1 or 2;  
m is 1 or 2;  
A is R<sup>2</sup>CO-, R<sup>3</sup>-O-CO-, or R<sup>4</sup>SO<sub>2</sub>-;

a group of the formula:



further wherein:

$R^1$  is a hydrogen atom, alkyl or phenylalkyl;

5  $R^2$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

$R^3$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

10  $R^4$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

15  $R^5$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

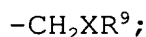
$R^6$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

5 R<sup>8</sup> is an amino acid side chain chosen from the group consisting of natural and unnatural amino acids;

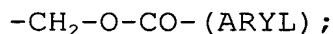
B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, (heteroaryl)alkyl, or halomethyl;

10 a group of the formula:

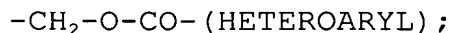


wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

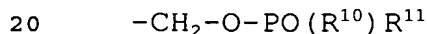
15 a group of the formula:



a group of the formula:



a group of the formula:



wherein R<sup>10</sup> and R<sup>11</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl and (substituted phenyl) alkyl; and the pharmaceutically-acceptable  
25 salts thereof.

233. (New) A method for reducing inflammation  
of a tissue, comprising contacting said tissue with an  
effective amount of a reagent that suppresses the  
protease activity of at least one member of the  
5 interleukin-1beta-converting enzyme (ICE)/CED-3 family,  
thereby reducing inflammation of said tissue.

234. (New) The method of claim 233, wherein  
said tissue is skin.

235. (New) The method of claim 234, wherein  
10 said tissue inflammation is due to trauma, sunburn,  
eczema, contact allergy, dermatitis, psoriasis,  
erysipelas, acne, ingrown nails, cuts, burns, insect  
bites, insect stings, or pruritus.

236. (New) The method of claim 233, wherein  
15 said tissue is mucosa.

237. (New) The method of claim 233, wherein  
said tissue inflammation is due to vaginitis,  
hemorrhoids, conjunctivitis, periodontitis, wisdom  
tooth eruption, teeth extraction, gingivitis,  
20 periodontal abscesses, or prosthesis.

238. (New) A method for ameliorating or  
treating infectious disease, comprising contacting a  
cell population with an inhibiting effective amount of  
a reagent that suppresses the protease activity of at  
25 least one member of the interleukin-1 beta-converting  
enzyme (ICE)/CED-3 family, thereby ameliorating or  
treating infectious disease.

239. (New) The method of claim 238, wherein said infectious disease is viral.

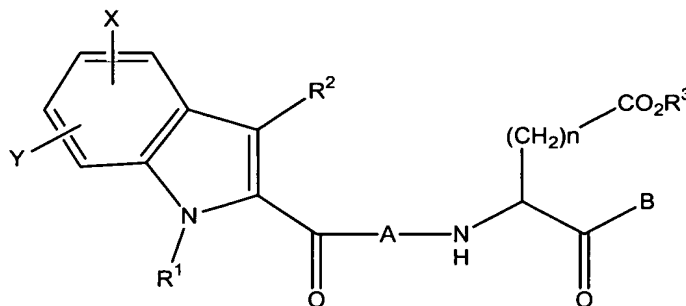
240. (New) The method of claim 238, wherein said contacting is in vitro.

5                   241. (New) The method of claim 238, wherein said contacting is in vivo.

242. (New) The method of claim 238, wherein the reagent suppresses the protease activity in an irreversible manner.

10                   243. (New) The method of claim 238, wherein the reagent suppresses the protease activity in a reversible manner.

244. (New) The method of claim 238, wherein the reagent is a compound of formula 1:



15                   FORMULA 1

wherein:

n is 1 or 2;



5 R<sup>1</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
or (CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup>, wherein m=1-4, and R<sup>4</sup> is as defined  
below;

10 R<sup>2</sup> is a hydrogen atom, chloro, alkyl,  
cycloalkyl, (cycloalkyl)alkyl,  
phenyl, (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
or (CH<sub>2</sub>)<sub>p</sub>CO<sub>2</sub>R<sup>5</sup>, wherein p=0-4, and R<sup>5</sup> is as defined  
below;

R<sup>3</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

15 R<sup>4</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

20 R<sup>5</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

A is a natural and unnatural amino acid;

25 B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl,  
phenyl, (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl, halomethyl, CH<sub>2</sub>ZR<sup>6</sup>, CH<sub>2</sub>OCO(aryl),  
CH<sub>2</sub>OCO(heteroaryl); or CH<sub>2</sub>OPO(R<sup>7</sup>)R<sup>8</sup>

where Z is an oxygen or a sulfur atom;

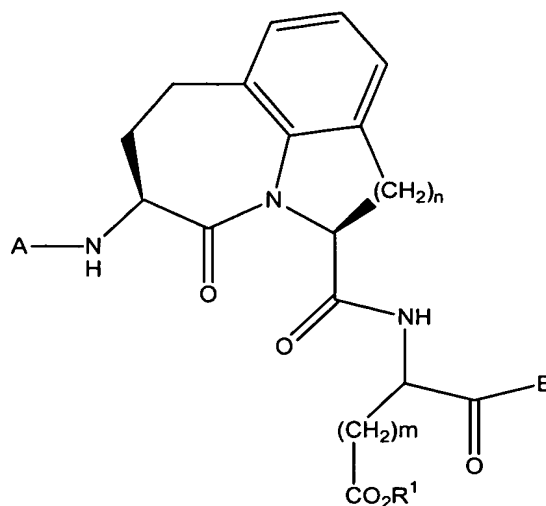
R<sup>6</sup> is phenyl, substituted phenyl, phenylalkyl, substituted phenylalkyl, heteroaryl, or (heteroaryl)alkyl; and

5 R<sup>7</sup> and R<sup>8</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl, (substituted phenyl) alkyl, and (cycloalkyl) alkyl; and

10 X and Y are independently selected from the group consisting of a hydrogen atom, halo, trihalomethyl, amino, protected amino, an amino salt, mono-substituted amino, di-substituted amino, carboxy, protected carboxy, a carboxylate salt, hydroxy, protected hydroxy, a salt of a hydroxy group, lower alkoxy, lower  
15 alkylthio, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, (cycloalkyl)alkyl, substituted (cycloalkyl)alkyl, phenyl, substituted phenyl, phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

20 245. (New) The method of claim 238, wherein the reagent is a compound of formula 3:



FORMULA 3

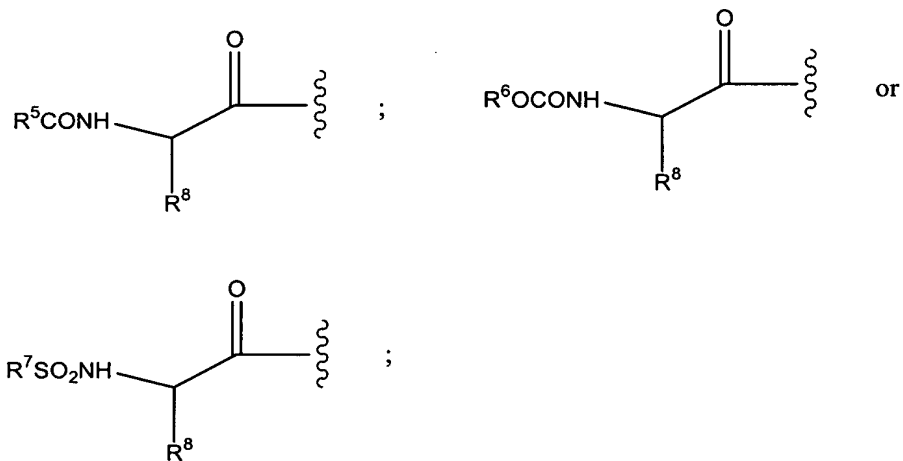
wherein:

n is 1 or 2;

m is 1 or 2;

5 A is  $R^2CO-$ ,  $R^3-CO-$ , or  $R^4SO_2-$ ;

a group of the formula:



further wherein:

$R^1$  is a hydrogen atom, alkyl or phenylalkyl;

R<sup>2</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

5 R<sup>3</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

R<sup>4</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

10 R<sup>5</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

15 R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>8</sup> is an amino acid side chain chosen from the group consisting of natural and unnatural amino acids;

20 B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, (heteroaryl)alkyl, or halomethyl;

a group of the formula:

--CH<sub>2</sub>XR<sup>9</sup>;

wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

a group of the formula:

5 -CH<sub>2</sub>-O-CO-(HETEROARYL);

a group of the formula:

-CH<sub>2</sub>-O-PO(R<sup>10</sup>)R<sup>11</sup>

wherein R<sup>10</sup> and R<sup>11</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl and (substituted phenyl) alkyl; and the pharmaceutically-acceptable salts thereof.

246. (New) A method for preventing or ameliorating inflammation due to an infectious disease comprising contacting a population of cells exposed to an infectious agent with an inhibiting effective amount of a reagent that suppresses the protease activity of at least one member of the interleukin-1 beta-converting enzyme (ICE)/CED-3 family.

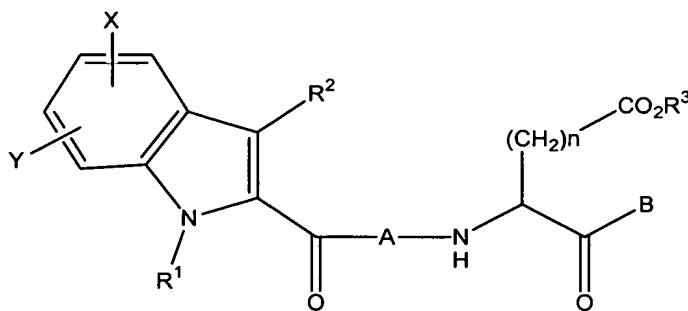
20 247. (New) The method of claim 246, wherein said contacting is in vitro.

248. (New) The method of claim 246, wherein said contacting is in vivo.

25 249. (New) The method of claim 246, wherein the reagent suppresses the protease activity in an irreversible manner.

250. (New) The method of claim 246, wherein the reagent suppresses the protease activity in a reversible manner.

251. (New) The method of claim 246, wherein  
5 the reagent is a compound of formula 1:



FORMULA 1

wherein:

- n is 1 or 2;
- 10  $R^1$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, (substituted)phenyl, phenylalkyl, (substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl or  $(CH_2)_mCO_2R^4$ , wherein  $m=1-4$ , and  $R^4$  is as defined below;
- 15  $R^2$  is a hydrogen atom, chloro, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, (substituted)phenyl, phenylalkyl, (substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl or  $(CH_2)_pCO_2R^5$ , wherein  $p=0-4$ , and  $R^5$  is as defined
- 20 below;

R<sup>3</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

5 R<sup>4</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

R<sup>5</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

10 A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl,  
phenyl, (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl,  
15 (heteroaryl)alkyl, halomethyl, CH<sub>2</sub>ZR<sup>6</sup>, CH<sub>2</sub>OCO(aryl),  
CH<sub>2</sub>OCO(heteroaryl); or CH<sub>2</sub>OPO(R<sup>7</sup>)R<sup>8</sup>

where Z is an oxygen or a sulfur atom;

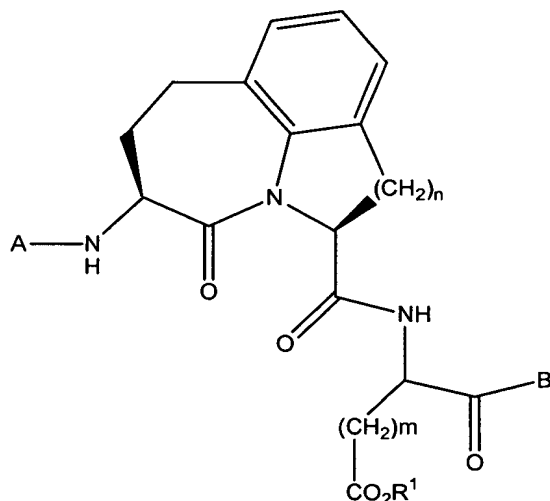
R<sup>6</sup> is phenyl, substituted phenyl, phenylalkyl,  
substituted phenylalkyl, heteroaryl, or  
20 (heteroaryl)alkyl; and

R<sup>7</sup> and R<sup>8</sup> are independently selected from a group  
consisting of alkyl, cycloalkyl, phenyl, substituted  
phenyl, phenylalkyl, (substituted phenyl) alkyl, and  
(cycloalkyl) alkyl; and

X and Y are independently selected from the group  
consisting of a hydrogen atom, halo, trihalomethyl,  
amino, protected amino, an amino salt, mono-substituted  
amino, di-substituted amino, carboxy, protected  
5 carboxy, a carboxylate salt, hydroxy, protected  
hydroxy, a salt of a hydroxy group, lower alkoxy, lower  
alkylthio, alkyl, substituted alkyl, cycloalkyl,  
substituted cycloalkyl, (cycloalkyl)alkyl, substituted  
(cycloalkyl)alkyl, phenyl, substituted phenyl,  
10 phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

252. (New) The method of claim 246, wherein  
the reagent is a compound of formula 3:



FORMULA 3

15 wherein:

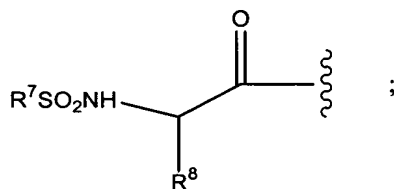
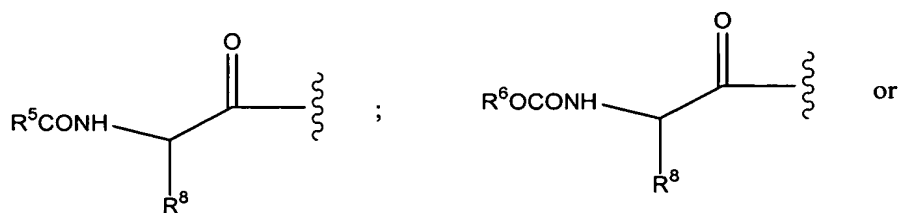
n is 1 or 2;



m is 1 or 2;

A is  $R^2CO-$ ,  $R^3-O-CO-$ , or  $R^4SO_2-$ ;

a group of the formula:



further

5

wherein:

$R^1$  is a hydrogen atom, alkyl or phenylalkyl;

$R^2$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
10 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

$R^3$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl,  
or (substituted phenyl)alkyl;

$R^4$  is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
15 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

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Supp. Amdt. dated March 11, 2004

R<sup>5</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

5 R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

10 R<sup>8</sup> is an amino acid side chain chosen from the group consisting of natural and unnatural amino acids;

B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, (heteroaryl)alkyl, or halomethyl;

15 a group of the formula:

--CH<sub>2</sub>XR<sup>9</sup>;

wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

20 a group of the formula:

-CH<sub>2</sub>-O-CO-(ARYL);

a group of the formula:

-CH<sub>2</sub>-O-CO-(HETEROARYL);

a group of the formula:

25 -CH<sub>2</sub>-O-PO(R<sup>10</sup>)R<sup>11</sup>

wherein R<sup>10</sup> and R<sup>11</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl and (substituted phenyl) alkyl; and the pharmaceutically-acceptable salts thereof.

253. (New) A method for preventing or treating inflammation-associated disorders, comprising contacting a cell population with an inhibiting effective amount of a reagent that suppresses the protease activity of at least one member of the interleukin-1beta-converting enzyme (ICE)/CED-3 family, thereby preventing or treating said inflammation-associated disorder.

254. (New) The method of claim 253, wherein said inflammation-associated disorder is due to an inflammatory disease.

255. (New) The method of claim 253, wherein said inflammation-associated disorder is asthma.

256. (New) The method of claim 253, wherein said inflammation-associated disorder is selected from the group consisting of pain, fever, asthma, bronchitis, vascular disease, nephrotic syndrome, and myocardial ischemia.

257. (New) The method of claim 253, wherein said inflammation-associated disorder is bronchitis.

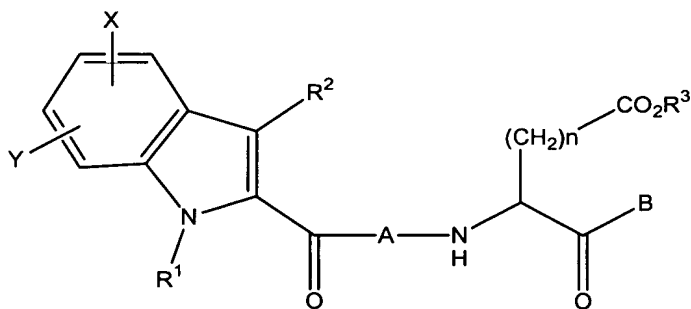
258. (New) The method of claim 253, wherein said inflammation-associated disorder is a vascular disease.

259. (New) The method of claim 256, wherein  
5 said pain is headache pain or joint pain.

260. (New) The method of claim 253, wherein the reagent suppresses the protease activity in an irreversible manner.

261. (New) The method of claim 253, wherein  
10 the reagent suppresses the protease activity in a reversible manner.

262. (New) The method of claim 253, wherein the reagent is a compound of formula 1:



FORMULA 1

15 wherein:

n is 1 or 2;

R<sup>1</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl

or  $(\text{CH}_2)_m\text{CO}_2\text{R}^4$ , wherein  $m=1-4$ , and  $\text{R}^4$  is as defined below;

$\text{R}^2$  is a hydrogen atom, chloro, alkyl,  
cycloalkyl, (cycloalkyl)alkyl,  
5 phenyl, (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
or  $(\text{CH}_2)_p\text{CO}_2\text{R}^5$ , wherein  $p=0-4$ , and  $\text{R}^5$  as defined below;

$\text{R}^3$  is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
10 (substituted)phenylalkyl;

$\text{R}^4$  is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or (substituted)phenyl  
alkyl;

$\text{R}^5$  is a hydrogen atom, alkyl, cycloalkyl,  
15 (cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl,  
20 phenyl, (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl, halomethyl,  $\text{CH}_2\text{ZR}^6$ ,  $\text{CH}_2\text{OCO}(\text{aryl})$ ,  
 $\text{CH}_2\text{OCO}(\text{heteroaryl})$ ; or  $\text{CH}_2\text{OPO}(\text{R}^7)\text{R}^8$  where Z is an oxygen  
or a sulfur atom;

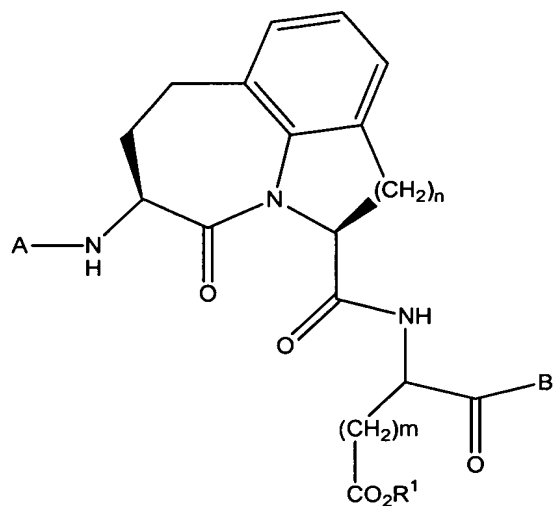
R<sup>6</sup> is phenyl, substituted phenyl, phenylalkyl, substituted phenylalkyl, heteroaryl, or (heteroaryl)alkyl; and

5 R<sup>7</sup> and R<sup>8</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl, (substituted phenyl) alkyl, and (cycloalkyl) alkyl; and

10 X and Y are independently selected from the group consisting of a hydrogen atom, halo, trihalomethyl, amino, protected amino, an amino salt, mono-substituted amino, di-substituted amino, carboxy, protected carboxy, a carboxylate salt, hydroxy, protected hydroxy, a salt of a hydroxy group, lower alkoxy, lower alkylthio, alkyl, substituted alkyl, cycloalkyl, 15 substituted cycloalkyl, (cycloalkyl)alkyl, substituted (cycloalkyl)alkyl, phenyl, substituted phenyl, phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

20 263. (New) The method of claim 253 wherein the reagent is a compound of formula 3:



FORMULA 3

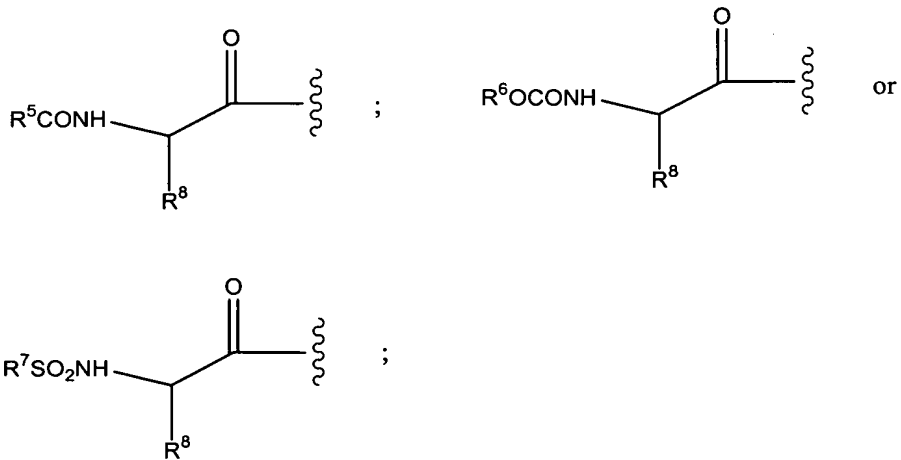
wherein:

n is 1 or 2;

m is 1 or 2;

5 A is R<sup>2</sup>CO-, R<sup>3</sup>-O-CO-, or R<sup>4</sup>SO<sub>2</sub>-;

a group of the formula:



further wherein:

R<sup>1</sup> is a hydrogen atom, alkyl or phenylalkyl;

R<sup>2</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

5 R<sup>3</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

R<sup>4</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

10 R<sup>5</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl, or (substituted phenyl)alkyl;

15 R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>8</sup> is an amino acid side chain chosen from the group consisting of natural and unnatural amino acids;

20 B is a hydrogen atom, a deuterium atom, alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl, substituted phenyl, (substituted phenyl)alkyl, heteroaryl, (heteroaryl)alkyl, or halomethyl;

a group of the formula:



--CH<sub>2</sub>XR<sup>9</sup>;

wherein R<sup>9</sup> is phenyl, substituted phenyl, phenylalkyl, (substituted phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

5 a group of the formula:

-CH<sub>2</sub>-O-CO-(ARYL);

a group of the formula:

-CH<sub>2</sub>-O-CO-(HETEROARYL);

a group of the formula:

10 -CH<sub>2</sub>-O-PO(R<sup>10</sup>)R<sup>11</sup>

wherein R<sup>10</sup> and R<sup>11</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl and (substituted phenyl) alkyl; and the pharmaceutically-acceptable  
15 salts thereof.

264. (New) The method of claim 253, wherein the cell population is also contacted with a second active agent.

265. (New) The method of claim 264, wherein  
20 the active agent is selected from the group consisting of: anti-inflammatory agents, matrix metalloprotease inhibitors, lipoxygenase inhibitors, antagonists of cytokines other than interleukin-1beta, agents that modify differentiation, agents that modify  
25 proliferation, agents that modify pigmentation, antibacterial agents, antiparasitic agents, antifungal agents, anaesthetics, antipruriginous agnets, antiviral

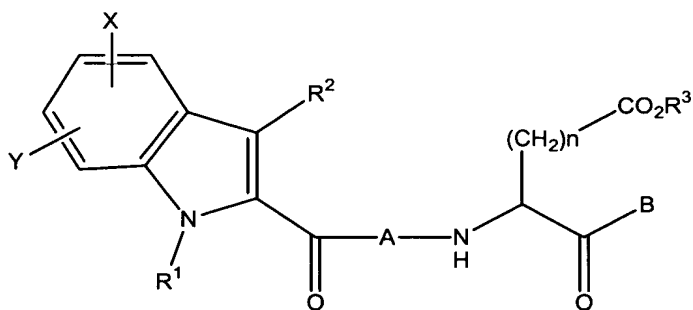
agents, keratolytic agents, anti-free-radical agents, anti-seborrhoeic agents, anti-dandruff agents, and anti-acne agents.

266. (New) A composition comprising a reagent  
5 that suppresses the protease activity of at least one member of the interleukin-1 $\beta$ -converting enzyme (ICE)/CED-3 family and an orally, nasally or intravenously acceptable carrier, adapted for preventing or treating inflammation-associated  
10 disorders.

267. (New) The composition of claim 266, wherein the reagent suppresses the protease activity in an irreversible manner.

268. (New) The composition of claim 266,  
15 wherein the reagent suppresses the protease activity in a reversible manner.

269. (New) The composition of claim 266, wherein the reagent is a compound of formula 1:



FORMULA 1

20 wherein:  
n is 1 or 2;

R<sup>1</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
(substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
or (CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>R<sup>4</sup>, wherein m=1-4, and R<sup>4</sup> is as defined  
5 below;

R<sup>2</sup> is a hydrogen atom, chloro, alkyl,  
cycloalkyl, (cycloalkyl)alkyl,  
phenyl, (substituted)phenyl, phenylalkyl,  
(substituted)phenylalkyl, heteroaryl, (heteroaryl)alkyl  
10 or (CH<sub>2</sub>)<sub>p</sub>CO<sub>2</sub>R<sup>5</sup>, wherein p=0-4, and R<sup>5</sup> is as defined  
below;

R<sup>3</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

15 R<sup>4</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
(substituted)phenylalkyl;

R<sup>5</sup> is a hydrogen atom, alkyl, cycloalkyl,  
(cycloalkyl)alkyl, phenylalkyl, or  
20 (substituted)phenylalkyl;

A is a natural and unnatural amino acid;

B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl,  
phenyl, (substituted)phenyl, phenylalkyl,  
25 (substituted)phenylalkyl, heteroaryl,  
(heteroaryl)alkyl, halomethyl, CH<sub>2</sub>ZR<sup>6</sup>, CH<sub>2</sub>OCO(aryl),  
CH<sub>2</sub>OCO(heteroaryl); or CH<sub>2</sub>OPO(R<sup>7</sup>)R<sup>8</sup>

where Z is an oxygen or a sulfur atom;

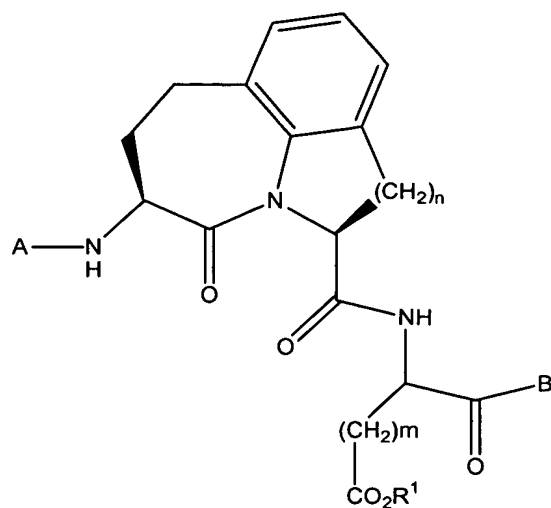
R<sup>6</sup> is phenyl, substituted phenyl, phenylalkyl, substituted phenylalkyl, heteroaryl, or (heteroaryl)alkyl; and

5 R<sup>7</sup> and R<sup>8</sup> are independently selected from a group consisting of alkyl, cycloalkyl, phenyl, substituted phenyl, phenylalkyl, (substituted phenyl) alkyl, and (cycloalkyl) alkyl; and

10 X and Y are independently selected from the group consisting of a hydrogen atom, halo, trihalomethyl, amino, protected amino, an amino salt, mono-substituted amino, di-substituted amino, carboxy, protected carboxy, a carboxylate salt, hydroxy, protected hydroxy, a salt of a hydroxy group, lower alkoxy, lower  
15 alkylthio, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, (cycloalkyl)alkyl, substituted (cycloalkyl)alkyl, phenyl, substituted phenyl, phenylalkyl, and (substituted phenyl)alkyl;

or a pharmaceutically acceptable salt thereof.

20 270. (New) The composition of claim 266, wherein the reagent is a compound of formula 3:



FORMULA 3

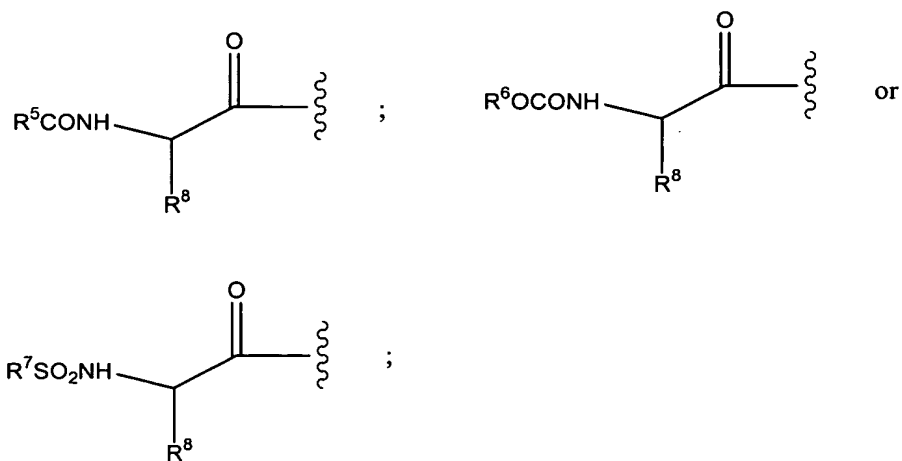
wherein:

n is 1 or 2;

m is 1 or 2;

5 A is  $R^2CO-$ ,  $R^3-O-CO-$ , or  $R^4SO_2-$ ;

a group of the formula:



further wherein:

R<sup>1</sup> is a hydrogen atom, alkyl or phenylalkyl;

R<sup>2</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl,  
phenyl, phenylalkyl, substituted phenyl, (substituted  
5 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>3</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl,  
or (substituted phenyl)alkyl;

R<sup>4</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
10 phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>5</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

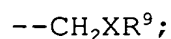
R<sup>6</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenylalkyl,  
15 or (substituted phenyl)alkyl;

R<sup>7</sup> is alkyl, cycloalkyl, (cycloalkyl)alkyl, phenyl,  
phenylalkyl, substituted phenyl, (substituted  
phenyl)alkyl, heteroaryl, or (heteroaryl)alkyl;

R<sup>8</sup> is an amino acid side chain chosen from the group  
20 consisting of natural and unnatural amino acids;

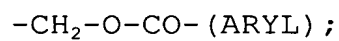
B is a hydrogen atom, a deuterium atom, alkyl,  
cycloalkyl, (cycloalkyl)alkyl, phenyl, phenylalkyl,  
substituted phenyl, (substituted phenyl)alkyl,  
heteroaryl, (heteroaryl)alkyl, or halomethyl;

a group of the formula:

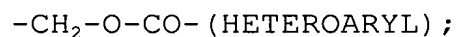


wherein  $\text{R}^9$  is phenyl, substituted phenyl, phenylalkyl,  
(substituted phenyl)alkyl, heteroaryl, or  
5 (heteroaryl)alkyl; and X is an oxygen or a sulfur atom;

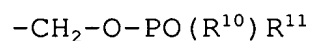
a group of the formula:



a group of the formula:



10 a group of the formula:



wherein  $\text{R}^{10}$  and  $\text{R}^{11}$  are independently selected from a  
group consisting of alkyl, cycloalkyl, phenyl,  
substituted phenyl, phenylalkyl and (substituted  
15 phenyl) alkyl; and the pharmaceutically-acceptable  
salts thereof.